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NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	OCT 02	CA/CAplus enhanced with pre-1907 records from Chemisches Zentralblatt
NEWS 3	OCT 19	BEILSTEIN updated with new compounds
NEWS 4	NOV 15	Derwent Indian patent publication number format enhanced
NEWS 5	NOV 19	WPIX enhanced with XML display format
NEWS 6	NOV 30	ICSD reloaded with enhancements
NEWS 7	DEC 04	LINPADOCDB now available on STN
NEWS 8	DEC 14	BEILSTEIN pricing structure to change
NEWS 9	DEC 17	USPATOLD added to additional database clusters
NEWS 10	DEC 17	IMSDRUGCONF removed from database clusters and STN
NEWS 11	DEC 17	DGENE now includes more than 10 million sequences
NEWS 12	DEC 17	TOXCENTER enhanced with 2008 MeSH vocabulary in MEDLINE segment
NEWS 13	DEC 17	MEDLINE and LMEDLINE updated with 2008 MeSH vocabulary
NEWS 14	DEC 17	CA/CAplus enhanced with new custom IPC display formats
NEWS 15	DEC 17	STN Viewer enhanced with full-text patent content from USPATOLD
NEWS 16	JAN 02	STN pricing information for 2008 now available
NEWS 17	JAN 16	CAS patent coverage enhanced to include exemplified prophetic substances
NEWS 18	JAN 28	USPATFULL, USPAT2, and USPATOLD enhanced with new custom IPC display formats
NEWS 19	JAN 28	MARPAT searching enhanced
NEWS 20	JAN 28	USGENE now provides USPTO sequence data within 3 days of publication
NEWS 21	JAN 28	TOXCENTER enhanced with reloaded MEDLINE segment
NEWS 22	JAN 28	MEDLINE and LMEDLINE reloaded with enhancements
NEWS 23	FEB 08	STN Express, Version 8.3, now available
NEWS 24	FEB 20	PCI now available as a replacement to DPCI
NEWS 25	FEB 25	IFIREF reloaded with enhancements
NEWS 26	FEB 25	IMSPRODUCT reloaded with enhancements
NEWS 27	FEB 29	WPINDEX/WPIDS/WPIX enhanced with ECLA and current U.S. National Patent Classification
NEWS 28	MAR 31	IFICDB, IFIPAT, and IFIUDB enhanced with new custom IPC display formats
NEWS 29	MAR 31	CAS REGISTRY enhanced with additional experimental spectra
NEWS 30	MAR 31	CA/CAplus and CASREACT patent number format for U.S. applications updated
NEWS 31	MAR 31	LPCI now available as a replacement to LDPCI
NEWS 32	MAR 31	EMBASE, EMBAL, and LEMBASE reloaded with enhancements

NEWS EXPRESS FEBRUARY 08 CURRENT WINDOWS VERSION IS V8.3,
AND CURRENT DISCOVER FILE IS DATED 20 FEBRUARY 2008

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 NEWS IPC8     For general information regarding STN implementation of IPC 8

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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
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=>
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```
chain nodes :
8  9
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ring nodes :
1  2  3  4  5  6
ring/chain nodes :
7
chain bonds :
2-9  3-8  5-7
ring bonds :
1-2  1-6  2-3  3-4  4-5  5-6
exact/norm bonds :
1-2  1-6  2-3  2-9  3-4  4-5  5-6  5-7
exact bonds :
3-8


Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:CLASS  8:CLASS  9:CLASS



L1      STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1              STR
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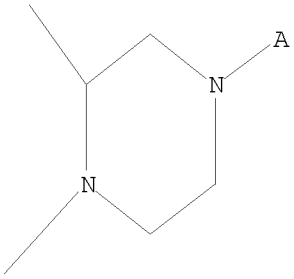


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Structure attributes must be viewed using STN Express query preparation.


=> l1 sss sam
SAMPLE SEARCH INITIATED 15:00:55 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -    10369 TO ITERATE

 19.3% PROCESSED     2000 ITERATIONS                                50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:       201277 TO   213483
PROJECTED ANSWERS:           45673 TO    51587

L2           50 SEA SSS SAM L1

=> l1 sss full
FULL SEARCH INITIATED 15:01:21 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -   207128 TO ITERATE

100.0% PROCESSED   207128 ITERATIONS                           48330 ANSWERS
SEARCH TIME: 00.00.01
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L3        48330 SEA SSS FUL L1

=> fil caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                     179.74     179.95

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FILE LAST UPDATED: 30 Mar 2008  (20080330/ED)

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=> l3
L4        7129 L3

=> peptid and l4
MISSING TERM BEFORE 'AND'
Search expressions cannot begin with operators.

=> peptid? and l4
        526193 PEPTID?
L5         594 PEPTID? AND L4

=> py>2001 and l5
       7539471 PY>2001
L6         356 PY>2001 AND L5

=> l5 not l6
L7         238 L5 NOT L6

=> peptidomimetic and l7
          3322 PEPTIDOMIMETIC
L8          24 PEPTIDOMIMETIC AND L7

=> d ibib abs l8 1-24

L8   ANSWER 1 OF 24  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:        2001:831902  CAPLUS
DOCUMENT NUMBER:         136:247758
TITLE:                   Synthesis and anti-HIV activity of glucose-containing
                         prodrugs derived from saquinavir, indinavir and
                         nelfinavir
```

AUTHOR(S): Rouquayrol, Marielle; Gaucher, Berangere; Greiner, Jacques; Aubertin, Anne-Marie; Vierling, Pierre; Guedj, Roger
CORPORATE SOURCE: Parc Valrose, Laboratoire de Chimie Bio-Organique, Universite de Nice Sophia-Antipolis, UMR 6001 CNRS, Nice, F-06108, Fr.
SOURCE: Carbohydrate Research (2001), 336(3), 161-180
CODEN: CRBRAT; ISSN: 0008-6215
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:247758

AB With the aim at improving the transport of the current HIV protease inhibitors across the intestinal and blood brain barriers and their penetration into the central nervous system, the synthesis of various acyl and carbamoyl glucose-containing prodrugs derived from saquinavir, indinavir and nelfinavir, their in vitro stability with respect to hydrolysis, and their anti-HIV activity have been investigated. D-Glucose, which is actively transported across these barriers, was connected through its 3-hydroxyl to these anti-proteases via a linker. The liberation of the active free drug during the incubation time of the prodrugs with the cells was found to be crucial for HIV inhibition. The labile ester linking of the glucose-containing moiety to the peptidomimetic hydroxyl of saquinavir or to the indinavir C-8 hydroxyl, which is not part of the transition state isostere, is not an obstacle for anti-HIV activity. This is not the case for its stable carbamate linking to the peptidomimetic hydroxyl of saquinavir, indinavir and nelfinavir. The chemical stability with respect to hydrolysis of some of the saquinavir and indinavir prodrugs reported here, the liberation rate of the active free drug and the HIV inhibitory potency are acceptable for an in vivo use of these prodrugs. These glucose-linked ester and carbamate prodrugs display a promising therapeutic potential provided that their bioavailability, penetration into the HIV sanctuaries, and/or the liberation of the active free drug from the carbamate prodrugs are improved. Furthermore, no cytotoxicity was detected for the prodrugs for concns. as high as 10 or even 100 μM, thus indicating an encouraging therapeutic index.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:678583 CAPLUS
DOCUMENT NUMBER: 136:48003
TITLE: Peptide mimetic HIV protease inhibitors are ligands for the orphan receptor SXR
AUTHOR(S): Dussault, Isabelle; Lin, Min; Hollister, Kevin; Wang, Eric H.; Synold, Timothy W.; Forman, Barry Marc
CORPORATE SOURCE: Division of Molecular Medicine, The Gonda Diabetes and Genetic Research Center, Beckman Research Institute, City of Hope National Medical Center, Duarte, CA, 91010, USA
SOURCE: Journal of Biological Chemistry (2001), 276(36), 33309-33312
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The orphan nuclear receptor SXR coordinately regulates drug clearance in response to a wide variety of xenobiotic compds. This signaling system protects the body from exposure to toxic compds.; however, it can also pose a severe barrier to drug therapy. We now demonstrate that the human

immunodeficiency virus (HIV) protease inhibitor ritonavir binds SXR and activates its target genes. This represents an example of a commonly used therapeutic agent that effectively activates SXR. We also show that other protease inhibitors are weaker (saquinavir) or unable to activate SXR (nelfinavir, indinavir) thus defining analogs that fail to induce SXR-regulated clearance pathways. Interestingly, HIV protease inhibitors are distinct from previously known SXR ligands in that they are peptide mimetic compds. This expands the ligand specificity of SXR to include this unique chemical class whose pharmaceutical significance is expanding. Finally, we show that SXR ligands activate expression of multiple resistance protein 2 (MRP2), a critical regulator of bile flow and biliary drug excretion. These findings have important implications for the role of SXR in regulating drug clearance and hepatic disorders associated with impaired bile flow.

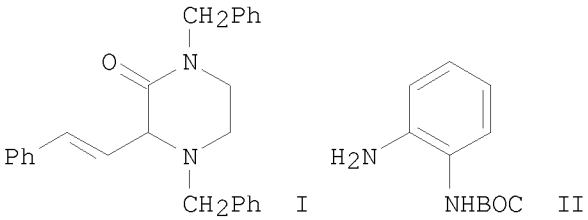
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

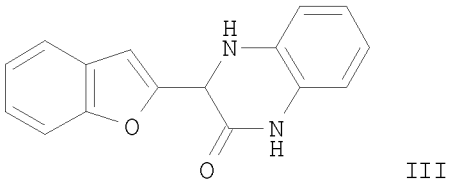
L8 ANSWER 3 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:122158 CAPLUS
DOCUMENT NUMBER: 134:311179
TITLE: 3,8-Diazabicyclo[3.2.1]octan-2-one Peptide Mimetics: Synthesis of a Conformationally Restricted Inhibitor of Farnesyltransferase
AUTHOR(S): Dinsmore, Christopher J.; Bergman, Jeffrey M.; Bogusky, Michael J.; Culberson, J. Christopher; Hamilton, Kelly A.; Graham, Samuel L.
CORPORATE SOURCE: Departments of Medicinal Chemistry Molecular Systems and Cancer Research, Merck Research Laboratories, West Point, PA, 19486, USA
SOURCE: Organic Letters (2001), 3(6), 865-868
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:311179

AB A new synthesis of the 3,8-diazabicyclo[3.2.1]octan-2-one framework is described. Transannular enolate alkylation of piperazinone derivs. provides a flexible route to highly constrained bicyclic peptidomimetic synthons with substitution at the Cα position. The chemical was used to produce a conformationally constrained farnesyltransferase inhibitor, which aided the elucidation of enzyme-bound conformation.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:897532 CAPLUS
DOCUMENT NUMBER: 134:147573
TITLE: Synthesis of piperazinones and benzopiperazinones from 1,2-diamines and organoboronic acids
AUTHOR(S): Petasis, N. A.; Patel, Z. D.
CORPORATE SOURCE: Department of Chemistry and Loker Hydrocarbon Research Institute, University of Southern California, Los Angeles, CA, 90089-1661, USA
SOURCE: Tetrahedron Letters (2000), 41(49), 9607-9611
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:147573
GI





III

AB Alkenyl, aryl and heteroaryl boronic acids, e.g. PhCH:CHB(OH)2, react with 1,2-diamines, e.g. PhCH2NHCH2CH2NHCH2Ph, and glyoxylic acid to give directly in one step the corresponding piperazinones, e.g. I. Similarly, the use of monoprotected 1,2-phenylenediamine, e.g. II, leads to benzopiperazinones, e.g. III.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:894543 CAPLUS

DOCUMENT NUMBER: 135:71099

TITLE: The fine tuning of high affinity and selective non-peptide agonists of the δ-opioid receptor via solution and solid-phase

AUTHOR(S): Alfaro-Lopez, Josue; Okayama, Toru; Hosohata, Keiko; Davis, Peg; Porreca, Frank; Yamamura, Henry I.; Hruby, Victor J.

CORPORATE SOURCE: Department of Chemistry, The University of Arizona, Tucson, AZ, 85721, USA

SOURCE: Peptides for the New Millennium, Proceedings of the American Peptide Symposium, 16th, Minneapolis, MN, United States, June 26-July 1, 1999 (2000), Meeting Date 1999, 38-39. Editor(s): Fields, Gregg B.; Tam, James P.; Barany, George. Kluwer Academic Publishers: Dordrecht, Neth.
CODEN: 69ATHX

DOCUMENT TYPE: Conference

LANGUAGE: English

AB A systematic approach to peptide and peptidomimetic design has been presented by Hruby et al. (Ann. N.Y. Acad. Sci., p. 7, volume 757, 1995). By applying this scheme to an ongoing research which seeks to translate the information contained in an endogenous opioid peptide such as enkephalin into a small organic compound, a series of new peptidomimetic compds. has been reported. The design was based on the topog. constrained and highly selective peptide [(2S,3R)TMT]DPDPE. SL-3111 (I) emerged as a promising non-peptidomimetic lead for further design, showing 8 nM binding affinity and over 2000-fold selectivity for bioassays, in spite of having a moderate selectivity of 460-fold μ/δ, it showed low potency. Efforts to improve the biol. profile of SL-3111, through the design and

synthesis of a second generation of peptidomimetics, are reported.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:812639 CAPLUS
DOCUMENT NUMBER: 134:71891
TITLE: Synthesis of chiral piperazinones as versatile scaffolds for peptidomimetics
AUTHOR(S): Rubsam, Frank; Mazitschek, Ralph; Giannis, Athanassios
CORPORATE SOURCE: Institut fur Organische Chemie der Universitat Karlsruhe, Karlsruhe, D-76128, Germany
SOURCE: Tetrahedron (2000), 56(43), 8481-8487
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:71891
AB Chiral piperazinones were synthesized as conformationally restricted peptidomimetics via reductive amination starting from inexpensive and readily available D-glucosamine hydrochloride and amino acid Me esters. Different synthetic strategies are devised to allow attachment of side chains imitating the parent peptide as shown for the RGD motif.
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:708749 CAPLUS
DOCUMENT NUMBER: 134:202449
TITLE: Tipranavir inhibits broadly protease inhibitor-resistant HIV-1 clinical samples
AUTHOR(S): Larder, Brendan A.; Hertogs, Kurt; Bloor, Stuart; van den Eynde, Ch.; DeCian, Wanda; Wang, Yenyun; Freimuth, William W.; Tarpley, Gary
CORPORATE SOURCE: Virco UK Ltd, Cambridge, UK
SOURCE: AIDS (London) (2000), 14(13), 1943-1948
CODEN: AIDSET; ISSN: 0269-9370
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The antiviral activity of tipranavir (TPV), a nonpeptide HIV-1 protease inhibitor (PI), was assessed in vitro on 134 clin. isolates with a wide range of resistance to currently available peptidomimetic PI. The susceptibility of all 134 variants was then retested simultaneously with 4 PI (indinavir, ritonavir, nelfinavir, saquinavir) plus TPV, using the Antivirogram assay. Of 105 viruses with >10-fold resistance to three of the 4 PI and an average of 6.1 PI mutations per sample, 95 (90%) were susceptible to TPV; 8 (8%) had 4-10-fold resistance to TPV and only 2 (2%) had >10-fold resistance. The substantial lack of PI cross-resistance to TPV shown by highly PI-resistant clin. isolates makes TPV an attractive new-generation HIV inhibitor.
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:535988 CAPLUS
DOCUMENT NUMBER: 133:267133
TITLE: New highly potent dipeptidic growth hormone secretagogues with low molecular weight
AUTHOR(S): Peschke, Bernd; Ankersen, Michael; Hansen, Thomas

Kruse; Hansen, Birgit Sehested; Lau, Jesper; Nielsen, Karin Kramer; Raun, Kirsten
CORPORATE SOURCE: Health Care Chemistry, Novo Nordisk A/S, Malov, 2760, Den.
SOURCE: European Journal of Medicinal Chemistry (2000), 35(6), 599-618
CODEN: EJMCA5; ISSN: 0223-5234
PUBLISHER: Editions Scientifiques et Medicales Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Based on NN703, low mol. weight growth hormone secretagogues (GHSs) with a reduced number of hydrogen binding sites were designed by removal of the C-terminal amide group. The compds. were highly potent in combination with high efficacy in a rat pituitary cell assay, being characterized with EC50 values down to 0.8 nM. Selected compds. were tested in in vivo animal models. The oral bioavailability in dogs was 16-44%. Also, the ED50 values of the compds. were determined both in dog and swine.
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:443462 CAPLUS
DOCUMENT NUMBER: 133:223022
TITLE: Solid supported high-throughput organic synthesis of peptide β-turn mimetics via tandem Petasis reaction/diketopiperazine formation
AUTHOR(S): Golebiowski, A.; Klopfenstein, S. R.; Chen, J. J.; Shao, X.
CORPORATE SOURCE: Health Care Research Center, Combinatorial Chemistry Group, Procter & Gamble Pharmaceuticals, Mason, OH, 45040-8006, USA
SOURCE: Tetrahedron Letters (2000), 41(25), 4841-4844
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 133:223022
AB High-throughput organic synthesis of bicyclic diketopiperazines, β-turn mimetics, is described. Starting from Merrifield resin-bound piperazine-2-carboxylate, first two side-chains are introduced via the Petasis reaction and subsequent amide bond formation. Unblocking the α-amino group of piperazine-2-carboxylate, Boc-N-protected α-amino acid coupling, and deprotection followed by cyclative cleavage introduces the remaining side-chains.
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:311662 CAPLUS
DOCUMENT NUMBER: 133:114640
TITLE: Synthesis and anti-HIV activity of prodrugs derived from saquinavir and indinavir
AUTHOR(S): Giorgio, Audrey Farese-Di; Rouquayrol, Marielle; Greiner, Jacques; Aubertin, Anne-Marie; Vierling, Pierre; Guedj, Roger
CORPORATE SOURCE: Laboratoire de Chimie Bio-Organique, ESA 6001 CNRS, Universite de Nice Sophia-Antipolis, Nice, 06108, Fr.
SOURCE: Antiviral Chemistry & Chemotherapy (2000), 11(2), 97-110
CODEN: ACCHEH; ISSN: 0956-3202
PUBLISHER: International Medical Press
DOCUMENT TYPE: Journal

LANGUAGE: English

AB With a view to improving the pharmacol. properties, safety and pharmacokinetic profiles of current protease inhibitors, the synthesis of various acyl-substituted saquinavir and indinavir prodrugs, their in vitro stability with respect to hydrolysis and their anti-HIV (LAI and HTLV IIIB) activity and cytotoxicity in CEM-SS and MT4 cells have been investigated. Hydrolysis of the ester bond and liberation of the active free drug was crucial for HIV inhibition: the faster the hydrolysis, the closer the anti-HIV activity was to that of the resp. parent drug. This is the case for most of the C-14-substituted indinavir and saquinavir derivs. (IC50 from 10 to 360 nM for ester half-lives of 90 min to 40 h). Concomitantly, the level of HIV inhibition is very low for the prodrugs for which hydrolysis is very slow. This is the case with the myristoyl or oleyl saquinavir esters, owing to the stable masking of the hydroxyl that is part of the peptidomimetic non-cleavable transition state isostere responsible for the inhibitory potency of saquinavir (and indinavir). In contrast, the anti-HIV activity of the monosubstituted C-8 indinavir prodrugs seems not to be correlated with their resistance to hydrolysis, as expected (the C-8 hydroxyl of indinavir is not involved in the transition state isostere). No cytotoxicity was detected for the indinavir and saquinavir prodrugs for concns. as high as 10 or even 100 μM, thus indicating promising therapeutic potential.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 11 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:296186 CAPLUS

DOCUMENT NUMBER: 133:105336

TITLE: Synthesis of a novel thyrotropin releasing hormone (TRH) analog incorporating a piperazin-2-one ring

AUTHOR(S): Bhatt, Ulhas; Just, George

CORPORATE SOURCE: Department of Chemistry, McGill University, Montreal, QC, H3A 2K6, Can.

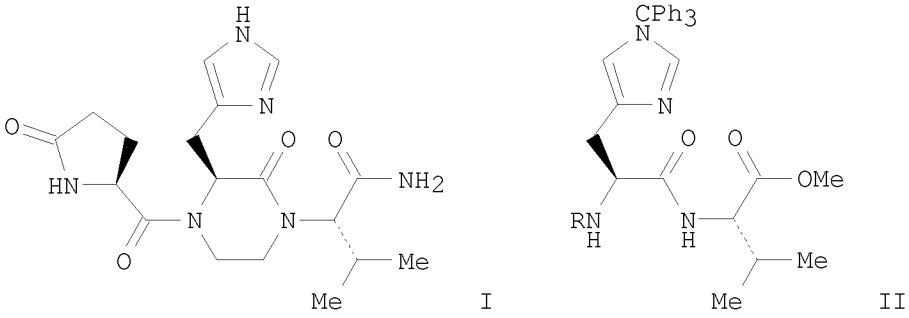
SOURCE: Helvetica Chimica Acta (2000), 83(4), 722-727
CODEN: HCACAV; ISSN: 0018-019X

PUBLISHER: Verlag Helvetica Chimica Acta

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



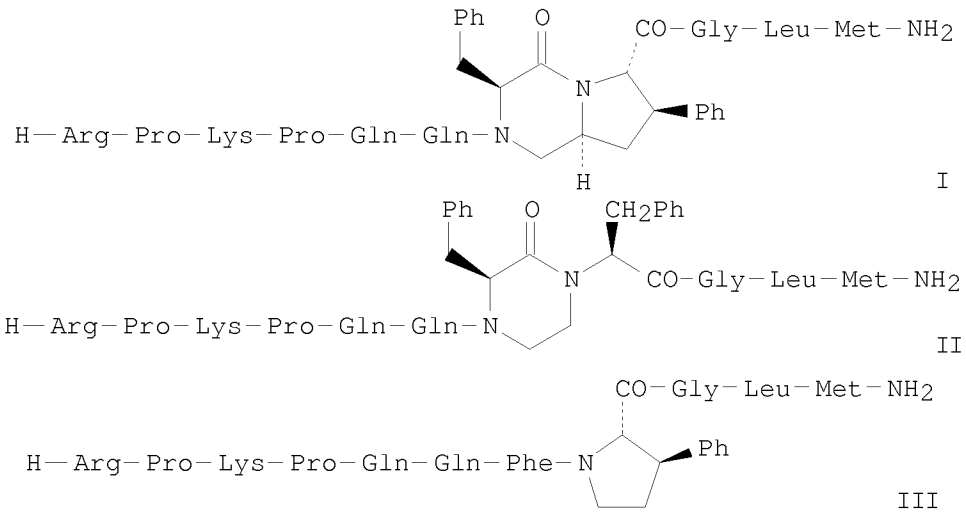
AB The synthesis of a TSH releasing hormone (TRH) analog, piperazinone-containing conformationally restricted peptidomimetic I, is described. The key recognition elements of the interaction between TRH and its receptor are retained in I. Synthesis of I started with dipeptide II (R = Fmoc) as the starting material, which was converted to its nitrobenzenesulfonylated derivative II (R = SO2C6H4NO2-4), followed by cyclization to the piperazinone derivative, N-acylation with L-pyroglutamate and deprotection to give I.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 12 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:276168 CAPLUS
DOCUMENT NUMBER: 133:53224
TITLE: Comparison of human immunodeficiency virus type 1 Pr55Gag and Pr160Gag-Pol processing intermediates that accumulate in primary and transformed cells treated with peptidic and nonpeptidic protease inhibitors
AUTHOR(S): Speck, R. Renae; Flexner, Charles; Tian, Chun-Juan; Yu, Xiao-Fang
CORPORATE SOURCE: Departments of Pharmacology and Molecular Sciences, The Johns Hopkins University School of Medicine, Baltimore, MD, 21287-5554, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2000), 44(5), 1397-1403
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Human immunodeficiency virus type 1 (HIV-1) produces two polyproteins, Pr55Gag and Pr160Gag-Pol, that are cleaved into mature functional subunits by the virally encoded protease. Drugs that inhibit this protease are an important part of anti-HIV therapy. We studied the ordered accumulation of Gag and Gag-Pol processing intermediates by variably blocking the protease with HIV-1 protease inhibitors (PIs). Variable protease inhibition caused accumulation of a complex pattern of processing intermediates, which was the same after incubating HIV-1-infected cells with increasing concns. of either one of the peptidomimetic inhibitors indinavir, saquinavir (SQV), ritonavir (RTV), nelfinavir, and SC-52151 or one of the nonpeptidomimetic inhibitors DMP450, DMP323, PNU-140135, and PNU-109112 for 3 days. The patterns of Gag and Gag-Pol processing intermediate accumulation were nearly identical when the following were compared: cell-vs. virion-associated proteins, HIV-1-infected transformed cell lines vs. primary human peripheral blood mononuclear cells (PBMCs) and HIV-1MN vs. HIV-1IIIB virus strains. RTV was a more potent inhibitor of p24 production in PBMCs than SQV by approx. 7-fold, whereas SQV was a more potent inhibitor in transformed cells than RTV by approx. 30-fold. Although the antiretroviral potency of HIV-1 PIs may change as a function of cell type, the polyprotein intermediates that accumulate with increasing drug concns. are the same. These results support sequential processing of Gag and Gag-Pol polyproteins by the HIV-1 protease and may have important implications for understanding common cross-resistance pathways.
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 13 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:188697 CAPLUS
DOCUMENT NUMBER: 133:4959
TITLE: Conformationally constrained substance P analogs: The total synthesis of a constrained peptidomimetic for the Phe7-Phe8 region
AUTHOR(S): Tong, Yunsong; Fobian, Yvette M.; Wu, Meiye; Boyd, Norman D.; Moeller, Kevin D.
CORPORATE SOURCE: The Department of Chemistry, Washington University, St. Louis, MO, 63130, USA
SOURCE: Journal of Organic Chemistry (2000), 65(8), 2484-2493
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society

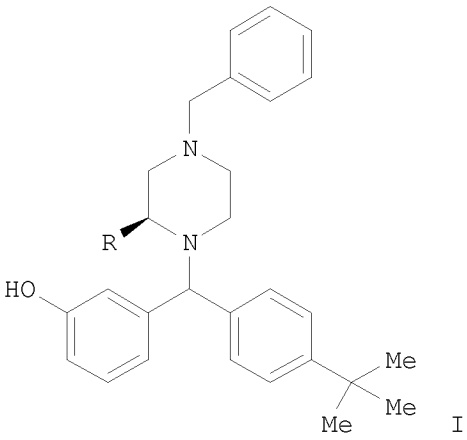
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB A bicyclic lactam I, peptidomimetic for the Phe7-Phe8 region of substance P, was synthesized. The synthesis used an anodic amide oxidation to selectively functionalize the C5-position of a 3-phenylproline derivative The resulting proline derivative was coupled to a Cbz-protected phenylalanine, and an intramol. reductive amination strategy used to convert the coupled material into a bicyclic piperazinone ring skeleton. The net result was a dipeptide building block that imbedded one of two proposed receptor bound conformations for the Phe7-Phe8 region of substance P into a bicyclic ring skeleton. The building block was then converted into a constrained substance P analog with the use of solid-phase peptide synthesis. A similar intramol. reductive amination strategy was used to synthesize a second substance P analog, piperazinone derivative II (only Phe7 constrained), and a third substance P analog, 3-phenylproline derivative III (only Phe8 constrained). All of the analogs were examined for their ability to displace substance P from its NK-1 receptor.
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 14 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:771172 CAPLUS
DOCUMENT NUMBER: 132:102411
TITLE: Exploring the Structure-Activity Relationships of [1-(4-tert-Butyl-3'-hydroxy)benzhydryl-4-benzylpiperazine] (SL-3111), A High-Affinity and Selective δ-Opioid Receptor Nonpeptide Agonist Ligand
AUTHOR(S): Alfaro-Lopez, Josue; Okayama, Toru; Hosohata, Keiko; Davis, Peg; Porreca, Frank; Yamamura, Henry I.; Hruby, Victor J.
CORPORATE SOURCE: Departments of Chemistry and Pharmacology, The University of Arizona, Tucson, AZ, 85721, USA
SOURCE: Journal of Medicinal Chemistry (1999), 42(26), 5359-5368
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

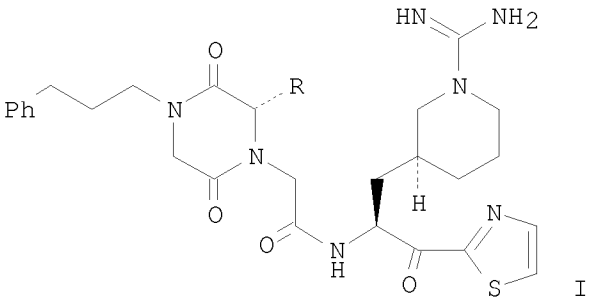


I

AB SL-3111 [1-(4-tert-butyl-3'-hydroxy)benzhydryl-4-benzylpiperazine] is a de novo designed, high-affinity and selective nonpeptide peptidomimetic agonist of the δ-opioid receptor. In a previous report we had described the unique biol. characteristics of this ligand and also a need for further structural evaluation. To pursue this, we have introduced a completely different heterocyclic template, which based on mol. modeling studies, may present the required structural features to properly orient the pharmacophore groups. We also have made more subtle changes to the original piperazine scaffold. The biol. activities of these compds. revealed an important participation of the scaffold in the ligand-receptor interaction. To further explore functional diversity on the scaffold, we have maintained the original piperazine ring and introduced four different functionalities at position 2 of the heterocyclic ring (I; R = CH2-O-CH2-Ph; R = Me; R = CH2Ph; R = CH2OH). The biol. activities observed for these compds. showed a very interesting trend in terms of the steric effects of the groups introduced at this position. A decrease of almost 2000-fold in affinity and potency at the δ-receptor was observed for I (R = CH2Ph) compared with I (R = Me). This difference may be explained if we postulate that the bioactive conformation of these peptidomimetics is close to the minimal energy conformations calculated in our study. On the basis of these findings we have realized the importance of this position to further explore and simplify the structure of future generations of peptidomimetic ligands.
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 15 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:614098 CAPLUS
DOCUMENT NUMBER: 132:3352
TITLE: The design of potent and selective inhibitors of thrombin utilizing a piperazinedione template. Part 1
AUTHOR(S): Cody, Wayne L.; Cai, Cuiman; Doherty, Annette M.; Edmunds, Jeremy J.; He, John X.; Narasimhan, Lakshmi S.; Plummer, Janet S.; Rapundalo, Stephen T.; Rubin, J. Ronald; Van Huis, Chad A.; St. Denis, Yves;

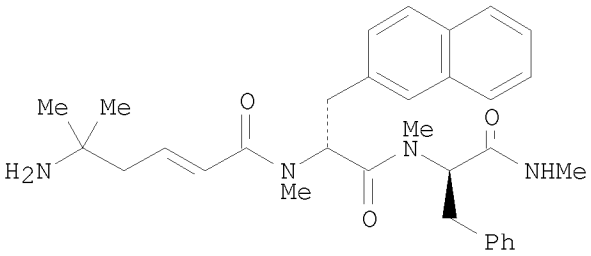
Winocour, Peter D.; Siddiqui, M. Arshad
CORPORATE SOURCE: Parke-Davis Pharmaceutical Research, Division of Warner-Lambert Company, Ann Arbor, MI, 48105, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1999), 9(17), 2497-2502
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



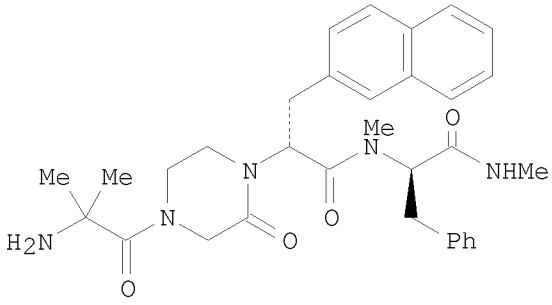
I

AB Utilizing X-ray crystallog. and mol. modeling, highly potent and selective peptidomimetic thrombin inhibitors have been designed containing a rigid piperazinedione template, I (R = CH2Ph, H, 3-pyridylmethyl, etc.). The synthesis and biol. activity of these compds. is described. The replacement of the benzyl group with aliphatic moieties led to compds. with reasonable selectivity for thrombin over trypsin. All of the compds. were relatively weak inhibitors. I [R = CH2(C6H11)] was the most potent among them.
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 16 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:292485 CAPLUS
DOCUMENT NUMBER: 131:32160
TITLE: Synthesis of piperazinones and their application in constrained mimetics of the growth hormone secretagogue NN-703
AUTHOR(S): Hansen, Thomas K.; Schlienger, Nathalie; Hansen, Birgit S.; Andersen, Peter H.; Bryce, Martin R.
CORPORATE SOURCE: Medicinal Chemistry Research, Novo Nordisk A/S, Malov, 2760, Den.
SOURCE: Tetrahedron Letters (1999), 40(18), 3651-3654
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I



II

AB The chemical of 2-piperazinones and the use of this building block to restrict the conformational freedom of the growth hormone secretagogue NN-703 (I; currently in clin. development) is reported here. The authors used classical methods for 2-piperazinone synthesis as well as some novel approaches such as a Boronic Mannich reaction. The authors, also, studied the ability of these constrained, piperazinone-based target compds. to release growth hormone in vitro. For example, piperazinone II was synthesized and was able to release growth hormone in-vitro at a concentration of 600 nM, compared to 18 nM concentration of I.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 17 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:548966 CAPLUS

DOCUMENT NUMBER: 129:276304

TITLE: Design and Synthesis of New Potent C2-Symmetric HIV-1 Protease Inhibitors. Use of L-Mannaric Acid as a Peptidomimetic Scaffold

AUTHOR(S): Alterman, Mathias; Bjoersne, Magnus; Muehlman, Anna; Classon, Bjoern; Kvarnstroem, Ingemar; Danielson, Helena; Markgren, Per-Olof; Nillroth, Ulrika; Unge, Torsten; Hallberg, Anders; Samuelsson, Bertil

CORPORATE SOURCE: Department of Chemistry, Linkoeping University, Linkoeping, S-581 83, Swed.

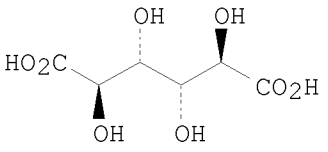
SOURCE: Journal of Medicinal Chemistry (1998), 41(20), 3782-3792
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

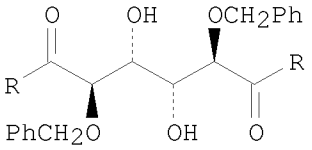
DOCUMENT TYPE: Journal

LANGUAGE: English

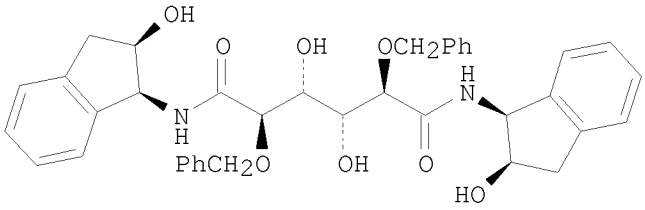
GI



I



II



III

AB A study on the use of derivatized carbohydrates as C2-sym. HIV-1 protease inhibitors has been undertaken. L-Mannaric acid (I) was bis-O-benzylated at C-2 and C-5 and subsequently coupled with amino acids and amines to give C2-sym. products based on C-terminal duplication. Potent HIV protease inhibitors, II (R = Val-NHMe) (Ki = 0.4 nM) and III (Ki = 0.2 nM), have been discovered, and two synthetic methodologies have been developed, one whereby these inhibitors can be prepared in just three chemical steps from com. available materials. A remarkable increase in potency going from II (R = Val-OMe) (IC50 = 5000 nM) to II (R = Val-NHMe) (IC50 = 15 nM) was observed, resulting in the net addition of one hydrogen bond interaction between each of the two NH groups and the HIV protease backbone (Gly 48/148). The x-ray crystal structures of III and of II (R = Ile-NHMe) have been determined, revealing the binding mode of these inhibitors which will aid further design.

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 18 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:497694 CAPLUS

DOCUMENT NUMBER: 129:227870

TITLE: Protein prenyl transferase activities of Plasmodium falciparum

AUTHOR(S): Chakrabarti, Debopam; Azam, Tania; DelVecchio, Cherie; Qiu, Libo; Park, Yong-il; Allen, Charles M.

CORPORATE SOURCE: Microbiology and Center for Diagnostics and Drug Development, Department of Molecular Biology, University of Central Florida, Orlando, FL, 322816-2360, USA

SOURCE: Molecular and Biochemical Parasitology (1998), 94(2), 175-184
CODEN: MBIPDP; ISSN: 0166-6851

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Prenylated proteins have been shown to function in important cellular regulatory processes, including signal transduction. The enzymes involved in protein prenylation, farnesyl transferase and geranylgeranyl transferase, have been recent targets for development of cancer chemotherapeutics. We have initiated a systematic study of protein prenyl transferases of the malaria parasite, Plasmodium falciparum, to determine whether these enzymes can be developed as targets for antimalarial chemotherapy. We report here the identification of protein farnesyl

transferase and protein geranylgeranyl transferase-I in the malaria parasite, P. falciparum. The farnesyl transferase has been partially purified from the cytosolic fraction through ammonium sulfate precipitation and Mono-Q chromatog. Farnesyl and geranylgeranyl transferase-I activities are present at all stages of P. falciparum intraerythrocytic development with maximum specific activity in the ring stage. Geranylgeranyl transferase-I specific activity is two times that of farnesyl transferase in the ring stage. Peptidomimetics and prenyl analogs of protein farnesyl transferase substrates were tested as in vitro inhibitors of partially purified P. falciparum prenyl transferase and of malaria parasite growth. The peptidomimetics were significantly more potent inhibitors than lipid substrate analogs of both the activity of Mono-Q purified enzyme and parasite growth in intraerythrocytic cultures. Exposure of the parasite to the peptidomimetic L-745,631 also showed significant inhibition of morphol. development beyond the trophozoite stage. These studies suggest the potential of designing or identifying differential inhibitors of P. falciparum and mammalian prenyl transferases as an approach to novel malaria therapy.

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 19 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:331224 CAPLUS

DOCUMENT NUMBER: 129:75969

TITLE: Transport characteristics of peptidomimetics . Effect of the pyrrolinone bioisostere on transport across Caco-2 cell monolayers

AUTHOR(S): Sudoh, Masao; Pauletti, Giovanni M.; Yao, Wenqing; Moser, William; Yokoyama, Akihisa; Pasternak, Alexander; Sprengeler, Paul A.; Smith, Amos B., III; Hirschmann, Ralph; Borchardt, Ronald T.

CORPORATE SOURCE: Department of Pharmaceutical Chemistry, The University of Kansas, Lawrence, KS, 66047, USA

SOURCE: Pharmaceutical Research (1998), 15(5), 719-725 CODEN: PHREEB; ISSN: 0724-8741

PUBLISHER: Plenum Publishing Corp.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB To compare the permeation characteristics of amide bond-containing HIV-1 protease inhibitors and their pyrrolinone-containing counterparts across Caco-2 cell monolayers, a model of the intestinal mucosa. Transepithelial transport and cellular uptake of three pairs of amide bond-containing and pyrrolinone-based peptidomimetics were assessed in the presence and absence of cyclosporin A using the Caco-2 cell culture model. The potential of the peptidomimetics to interact with biol. membranes was estimated by IAM chromatog. In the absence of cyclosporin A, apical (AP) to basolateral (BL) flux of all compds. studied was less than the flux determined in the opposite direction (i.e., BL-to-AP). The ratio of the apparent permeability coeffs. (Papp) calculated for the BL-to-AP and AP-to-BL transport (PBL→AP/PAP→BL) varied between 1.7 and 36.2. When individual pairs were compared, PBL→AP/PAP→BL ratios of the pyrrolinone-containing compds. were 1.5 to 11.5 times greater than those determined for the amide bond-containing analogs. Addition of 25 μM cyclosporin A to the transport buffer reduced the PBL→AP/PAP→BL ratios for all protease inhibitors to a value close to unity. Under these conditions, the amide bond-containing peptidomimetics were at least 1.6 to 2.8 times more able to permeate Caco-2 cell monolayers than were the pyrrolinone-containing compds. The intrinsic uptake characteristics into Caco-2 cells determined in the presence of 25 μM cyclosporin A were slightly greater for the amide bond-containing protease inhibitors than for the pyrrolinone-containing analogs.

These uptake results are consistent with the transepithelial transport results determined across this in vitro model of the intestinal mucosa.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 20 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:5383 CAPLUS

DOCUMENT NUMBER: 128:102361

TITLE: Synthesis and opiate activity of pseudo-tetrapeptides containing chiral piperazin-2-one and piperazine derivatives

AUTHOR(S): Yamashita, Tetsushi; Tsuru, Eiji; Banjyo, Eri; Doe, Matsumi; Shibata, Kozo; Yasuda, Masahide; Gemba, Munekazu

CORPORATE SOURCE: Department of Chemistry, Faculty of Science, Osaka City University, Osaka, 558, Japan

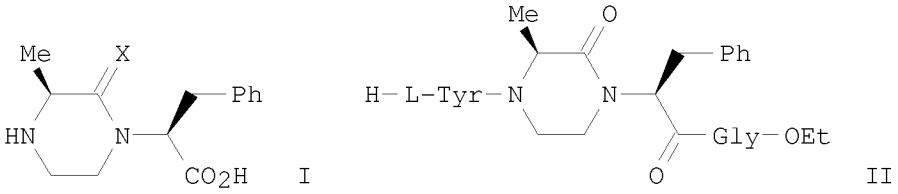
SOURCE: Chemical & Pharmaceutical Bulletin (1997), 45(12), 1940-1944
CODEN: CPBTAL; ISSN: 0009-2363

PUBLISHER: Pharmaceutical Society of Japan

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



AB Enantiomeric piperazin-2-one derivs., N,N'-ethylene-bridged alanylphenylalanines, e.g. I (X = O), were prepared using L- or D-Ala and L- or D-Phe as starting materials, and were inserted into the second and third positions of enantiomeric pseudotetrapeptides, e.g. II. The corresponding piperazine derivs., e.g. I (X = H2) were obtained by selective BH3 reduction of the amide carbonyl groups and similarly inserted into the same positions of the tetrapeptides. Enantiomeric N,N'-ethylene-bridged Tyr-Tyr derivs., obtained from L- or D-Tyr, were also inserted into the first and second positions of two pairs of enantiomeric tetrapeptides. The opiate activities of the 8 peptides thus obtained were studied by use of the mouse vas deferens and the guinea pig ileum assays in order to elucidate the structure-activity relationships of these peptides, especially with respect to stereochem.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 21 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1997:740109 CAPLUS

DOCUMENT NUMBER: 128:13146

TITLE: Preparation of norbornene-containing peptide analogs as HIV protease inhibitors useful for the treatment of AIDS

INVENTOR(S): Hungate, Randall W.; Kim, Byeong Moon; Vacca, Joseph P.

PATENT ASSIGNEE(S): Kim, Byeong Moon, USA; Vacca, Joseph P.; Merck & Co., Inc.; Hungate, Randall W.

SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9740825	A1	19971106	WO 1997-US6595	19970429
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2252918	A1	19971106	CA 1997-2252918	19970429
AU 9729238	A	19971119	AU 1997-29238	19970429
AU 711713	B2	19991021		
EP 912170	A1	19990506	EP 1997-923431	19970429
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2000509389	T	20000725	JP 1997-538974	19970429

PRIORITY APPLN. INFO.:

US 1996-16685P	P	19960502
GB 1996-13488	A	19960627
WO 1997-US6595	W	19970429

OTHER SOURCE(S): MARPAT 128:13146
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I and II [R, R1 = independently H, (un)substituted C3-5 cycloalkyl, (un)substituted aryl, C1-4 alkyl (un)substituted with halo, OH, C1-3 alkoxy, (un)substituted aryl, W-aryl, W-benzyl, (un)substituted heterocycle, CO2H; W = O, S, NH; RR1 form 4-6 membered ring; R2 = H, (un)substituted Ph, (un)substituted C5-7 cycloalkyl, C1-4 alkyl; R3 = CH2NR5R6, fragment X; R4 = (un)substituted 5-7-membered heterocycle, (un)substituted aryl, (un)substituted C1-4 alkyl, (un)substituted C3-5 cycloalkyl; R5 = VR4; V = COQ, SO2Q; Q = bond, O, NH; R6 = H, (un)substituted C1-4 alkyl, (un)substituted C3-5 cycloalkyl, (un)substituted aryl; J = any group Q1-Q3], and pharmaceutically acceptable salts thereof, are HIV protease inhibitors. These compds. are useful in the prevention or treatment of infection by HIV and in the treatment of AIDS, either as compds., pharmaceutically acceptable salts, pharmaceutical composition ingredients, whether or not in combination with other antivirals, immunomodulators, antibiotics or vaccines. Methods of treating AIDS and methods of preventing or treating infection by HIV are also described. Thus, amidation of norbornene III (preparation given) with indane-containing peptide mimic IV (preparation given) gave 39% norbornene pentaneamide V. Prepared compound V inhibited microbial expressed HIV protease with IC50 = 0.055 nM.

L8 ANSWER 22 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:156459 CAPLUS
DOCUMENT NUMBER: 126:258416
TITLE: Pharmacokinetic enhancement of inhibitors of the human immunodeficiency virus protease by coadministration with ritonavir
AUTHOR(S): Kempf, Dale J.; Marsh, Kennan C.; Kumar, Gondi;

Rodrigues, A. David; Denissen, Jon F.; McDonald, Edith; Kukulka, Michael J.; Hsu, Ann; Granneman, G. Richard; Baroldi, Paolo A.; Sun, Eugene; Pizzuti, David; Plattner, Jacob J.; Norbeck, Daniel W.; Leonard, John M.

CORPORATE SOURCE: Dep. Infectious Diseases Res., Abbott Lab., Abbott Park, IL, 60064, USA

SOURCE: Antimicrobial Agents and Chemotherapy (1997), 41(3), 654-660
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Coadministration with the human immunodeficiency virus (HIV) protease inhibitor ritonavir was investigated as a method for enhancing the levels of other peptidomimetic HIV protease inhibitors in plasma. In rat and human liver microsomes, ritonavir potently inhibited the cytochrome P 450 (CYP)-mediated metabolism of saquinavir, indinavir, nelfinavir, and VX-478. The structural features of ritonavir responsible for CYP binding and inhibition were examined Coadministration of other protease inhibitors with ritonavir in rats and dogs produced elevated and sustained plasma drug levels 8 to 12 h after a single dose. Drug exposure in rats was elevated by 8- to 46-fold. A >50-fold enhancement of the concns. of saquinavir in plasma was observed in humans following a single co-dose of ritonavir (600 mg) and saquinavir (200 mg). These results indicate that ritonavir can favorably alter the pharmacokinetic profiles of other protease inhibitors. Combination regimens of ritonavir and other protease inhibitors may thus play a role in the treatment of HIV infection. Because of potentially substantial drug level increases, however, such combinations require further investigation to establish safe regimens for clin. use.

L8 ANSWER 23 OF 24 CAPLUS

ACCESSION NUMBER: 1996:601709 CAPLUS
DOCUMENT NUMBER: 125:238651

TITLE: Use of quinoxalines and protease inhibitors in a composition for the treatment of AIDS and/or HIV infections

INVENTOR(S): Paessens, Arnold; Blunck, Martin; Riess, Guenther; Kleim, Joerg-Peter; Roesner, Manfred

PATENT ASSIGNEE(S): Bayer A.-G., Germany

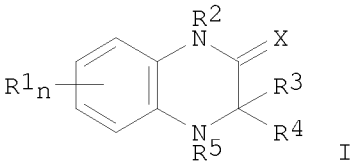
SOURCE: Eur. Pat. Appl., 24 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 728481	A2	19960828	EP 1996-102129	19960214
EP 728481	A3	19980708		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
DE 19506742	A1	19960829	DE 1995-19506742	19950227
AU 9645615	A	19960905	AU 1996-45615	19960220
AU 710158	B2	19990916		
CA 2170222	A1	19960828	CA 1996-2170222	19960223
FI 9600850	A	19960828	FI 1996-850	19960223
JP 08245392	A	19960924	JP 1996-60286	19960223
IL 117247	A	20001031	IL 1996-117247	19960223
NO 9600775	A	19960828	NO 1996-775	19960226
ZA 9601516	A	19960903	ZA 1996-1516	19960226

HU 9600455	A2	19961230	HU 1996-455	19960226
HU 9600455	A3	19980428		
BR 9600809	A	19971223	BR 1996-809	19960226
CN 1141196	A	19970129	CN 1996-102709	19960227

PRIORITY APPLN. INFO.: DE 1995-19506742 A 19950227
OTHER SOURCE(S): MARPAT 125:238651
GI



I

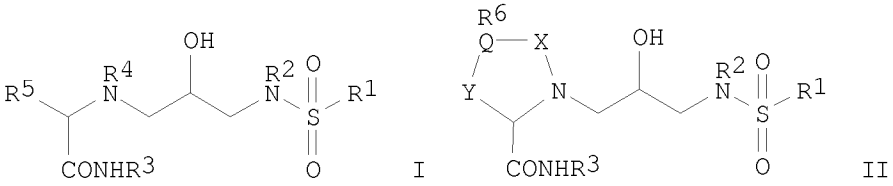
AB Combinations of a quinoxaline derivative [I; R1 = halo, OH, NO2, (substituted) amino, N3, CF3, CF3O, C1-8 alkyl, CN, (substituted) Ph, N-heterocyclyl, etc.; R2, R5 = H, OH, C1-6 alkoxy, aryloxy, C1-6 acyloxy, CN, (substituted) amino, (substituted) C1-8 alkyl, (substituted) C2-8 alkenyl, (substituted) C3-8 alkynyl, (substituted) C3-8 cycloalk(en)yl, etc.; R3, R4 = H, (substituted) C1-8 alkyl, (substituted) C2-8 alkenyl, (substituted) C3-8 cycloalk(en)yl, (substituted)aryl, etc.; or R3R4 or R3R5 complete a (substituted) ring; X = O, S, Se, NR2; n = 0-4] and a peptidomimetic protease inhibitor are useful for treatment of HIV infections and AIDS. Thus, I [R1 = 6-MeO, R2 = R3 = H, R4 = (S)-MeSCH2, R5 = i-PrO2C, X = S] (0.7-6 nM) and saquinavir (6-50 nM) synergistically inhibited syncytium formation in HIV-infected human lymphocytes in vitro.

L8 ANSWER 24 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1996:366115 CAPLUS
DOCUMENT NUMBER: 125:115158
TITLE: Peptidomimetic N-(2-hydroxy-3-aminopropyl)sulfonamides as proteolytic enzyme inhibitors
INVENTOR(S): Sprengeler, Paul; Smith, Amos B., III; Hirschmann, Ralph F.; Yokoyama, Akihisa
PATENT ASSIGNEE(S): University of Pennsylvania, USA
SOURCE: U.S., 9 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5519060	A	19960521	US 1995-373564	19950117
WO 9622087	A1	19960725	WO 1996-US501	19960116

W: CA, JP
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: US 1995-373564 A 19950117
OTHER SOURCE(S): MARPAT 125:115158
GI



I II

AB A method is claimed for modulating the activity of an enzyme (no data), comprising contacting said enzyme with at least one compound having structure I or II: wherein: R1 is H, OH, alkyl having 1 to about 10 carbon atoms, or aryl having 3 to about 20 carbon atoms; R2 is H, alkyl having 1 to about 10 carbon atoms, aryl having 3 to about 20 carbon atoms, alkaryl having 4 to about 25 carbon atoms, or an amino acid side chain; R3 is H, alkyl having one to about 10 carbon atoms, or alkaryl having 4 to about 25 carbon atoms; R4 is H, alkyl having 1 to about 10 carbon atoms, aryl having 3 to about 20 carbon atoms, alkaryl having 4 to about 25 carbon atoms, or an amino acid side chain; R5 is H, alkyl having one to about 10 carbon atoms, or aryl having 3 to about 20 carbon atoms; R6 is H, alkyl having one to about 10 carbon atoms, aryl having 3 to about 20 carbon atoms, or alkaryl having 4 to about 25 carbon atoms; X and Y are, independently, alkylene having 1 to about 6 carbon atoms, provided that the sum of X and Y is less than or equal to 9; and Q is N or CH2. Synthetic schemes for the preparation of representative II structures are provided.

=> d fbib abs hitstr l8 1-24

L8 ANSWER 1 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2001:831902 CAPLUS
DN 136:247758
TI Synthesis and anti-HIV activity of glucose-containing prodrugs derived from saquinavir, indinavir and nelfinavir
AU Rouquayrol, Marielle; Gaucher, Berangere; Greiner, Jacques; Aubertin, Anne-Marie; Vierling, Pierre; Guedj, Roger
CS Parc Valrose, Laboratoire de Chimie Bio-Organique, Universite de Nice Sophia-Antipolis, UMR 6001 CNRS, Nice, F-06108, Fr.
SO Carbohydrate Research (2001), 336(3), 161-180
CODEN: CRBRAT; ISSN: 0008-6215
PB Elsevier Science Ltd.
DT Journal
LA English
OS CASREACT 136:247758
AB With the aim at improving the transport of the current HIV protease inhibitors across the intestinal and blood brain barriers and their penetration into the central nervous system, the synthesis of various acyl and carbamoyl glucose-containing prodrugs derived from saquinavir, indinavir and nelfinavir, their in vitro stability with respect to hydrolysis, and their anti-HIV activity have been investigated. D-Glucose, which is actively transported across these barriers, was connected through its 3-hydroxyl to these anti-proteases via a linker. The liberation of the active free drug during the incubation time of the prodrugs with the cells was found to be crucial for HIV inhibition. The labile ester linking of the glucose-containing moiety to the peptidomimetic hydroxyl of saquinavir or to the indinavir C-8 hydroxyl, which is not part of the transition state isostere, is not an obstacle for anti-HIV activity. This is not the case for its stable carbamate linking to the peptidomimetic hydroxyl of saquinavir, indinavir and nelfinavir.

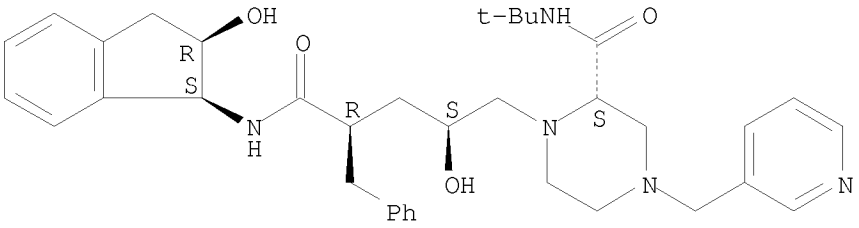
The chemical stability with respect to hydrolysis of some of the saquinavir and indinavir prodrugs reported here, the liberation rate of the active free drug and the HIV inhibitory potency are acceptable for an in vivo use of these prodrugs. These glucose-linked ester and carbamate prodrugs display a promising therapeutic potential provided that their bioavailability, penetration into the HIV sanctuaries, and/or the liberation of the active free drug from the carbamate prodrugs are improved. Furthermore, no cytotoxicity was detected for the prodrugs for concns. as high as 10 or even 100 μM, thus indicating an encouraging therapeutic index.

IT 150378-17-9, Indinavir
RL: PAC (Pharmacological activity); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(synthesis and anti-HIV activity of glucose-containing prodrugs derived from saquinavir, indinavir, and nelfinavir)

RN 150378-17-9 CAPLUS

CN D-erythro-Pentonamide, 2,3,5-trideoxy-N-[(1S,2R)-2,3-dihydro-2-hydroxy-1H-inden-1-yl]-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)- (CA INDEX NAME)

Absolute stereochemistry.



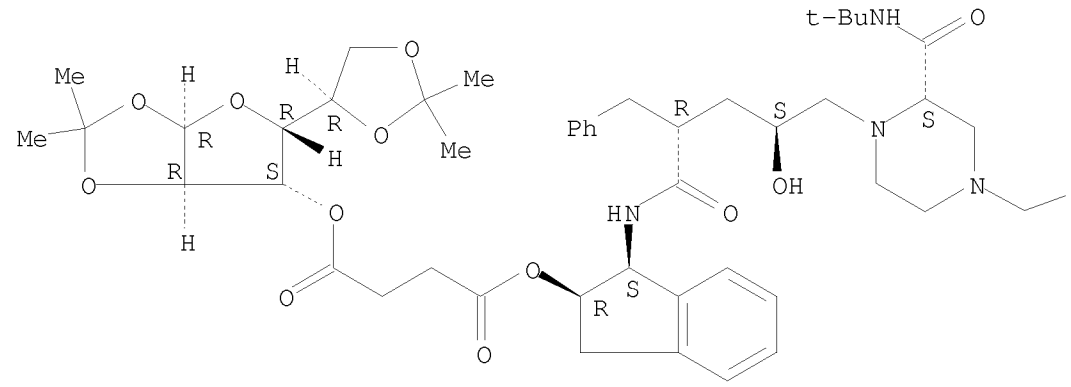
IT 404001-83-8P 404001-94-1P 404001-98-5P
404002-02-4P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and anti-HIV activity of glucose-containing prodrugs derived from saquinavir, indinavir, and nelfinavir)

RN 404001-83-8 CAPLUS

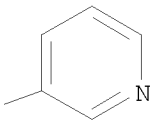
CN α-D-Glucofuranose, 1,2:5,6-bis-O-(1-methylethylidene)-, (1S,2R)-2,3-dihydro-1-[[2,3,5-trideoxy-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)-D-erythro-pentonoyl]amino]-1H-inden-2-yl butanedioate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

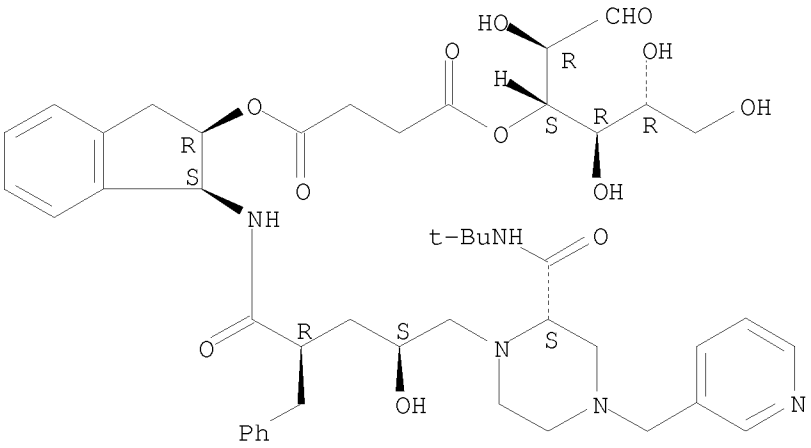


RN 404001-94-1 CAPLUS
CN D-Glucose, 3-[(1S,2R)-2,3-dihydro-1-[[2,3,5-trideoxy-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)-D-erythro-pentonoyl]amino]-1H-inden-2-yl butanedioate], tris(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

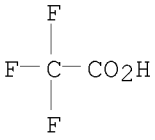
CRN 404001-93-0
CMF C46 H61 N5 O12

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

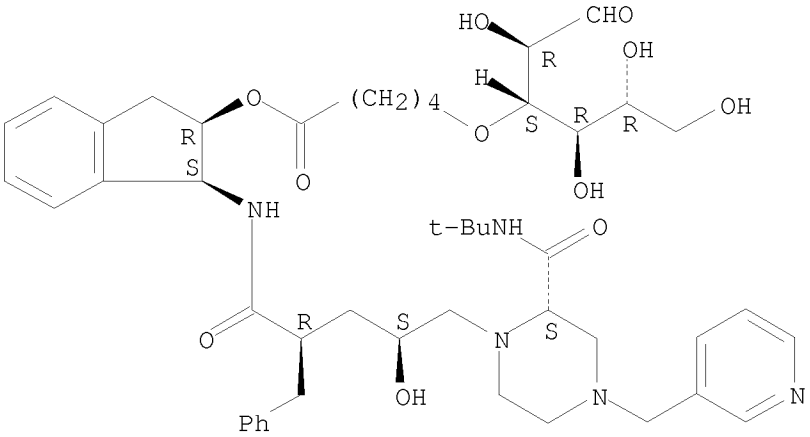


RN 404001-98-5 CAPLUS
CN D-Glucose, 3-O-[5-[[(1S,2R)-2,3-dihydro-1-[[2,3,5-trideoxy-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)-D-erythro-pentonoyl]amino]-1H-inden-2-yl]oxy]-5-oxopentyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

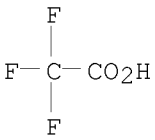
CRN 404001-97-4
CMF C47 H65 N5 O11

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



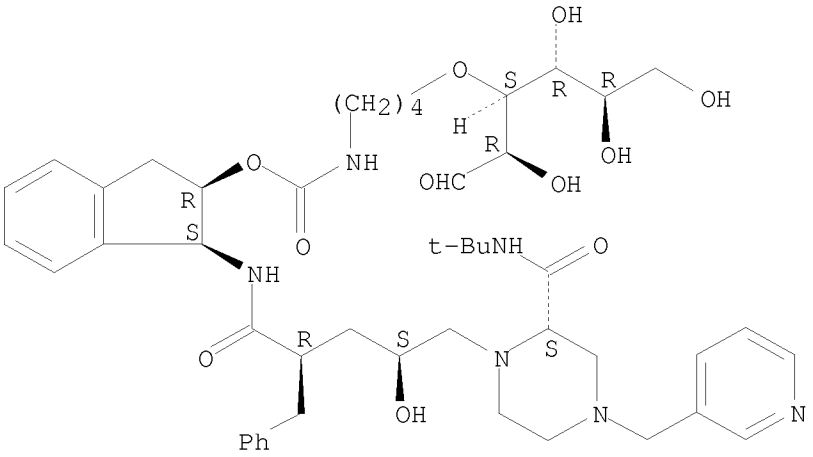
RN 404002-02-4 CAPLUS
CN D-Glucose, 3-O-[4-[[[[(1S,2R)-2,3-dihydro-1-[[2,3,5-trideoxy-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)-D-erythro-pentonoyl]amino]-1H-inden-2-yl]oxy]carbonyl]amino]butyl]-, bis(trifluoroacetate) (salt) (9CI) (CA

INDEX NAME)

CM 1

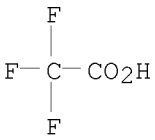
CRN 404002-01-3
CMF C47 H66 N6 O11

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



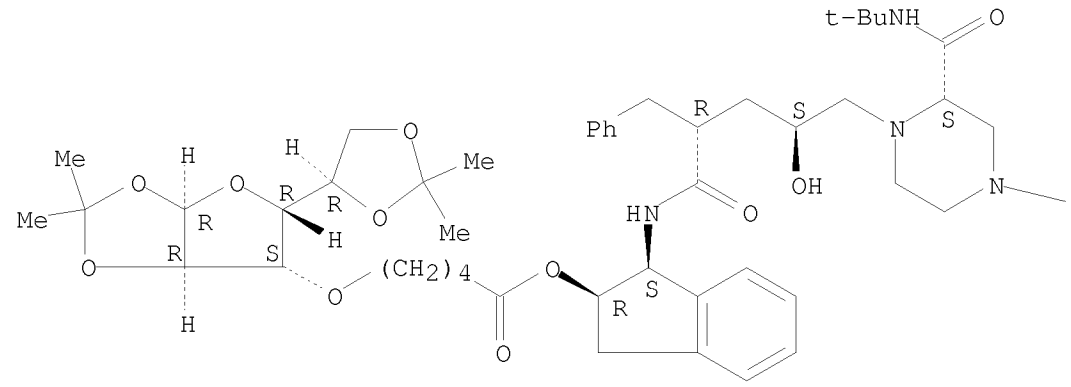
IT 404001-87-2P 404001-89-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and anti-HIV activity of glucose-containing prodrugs derived from saquinavir, indinavir, and nelfinavir)

RN 404001-87-2 CAPLUS

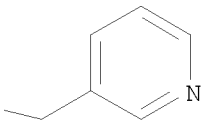
CN α-D-Glucofuranose, 3-O-[5-[[(1S,2R)-2,3-dihydro-1-[[2,3,5-trideoxy-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)-D-erythro-pentonoyl]amino]-1H-inden-2-yl]oxy]-5-oxopentyl]-1,2:5,6-bis-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

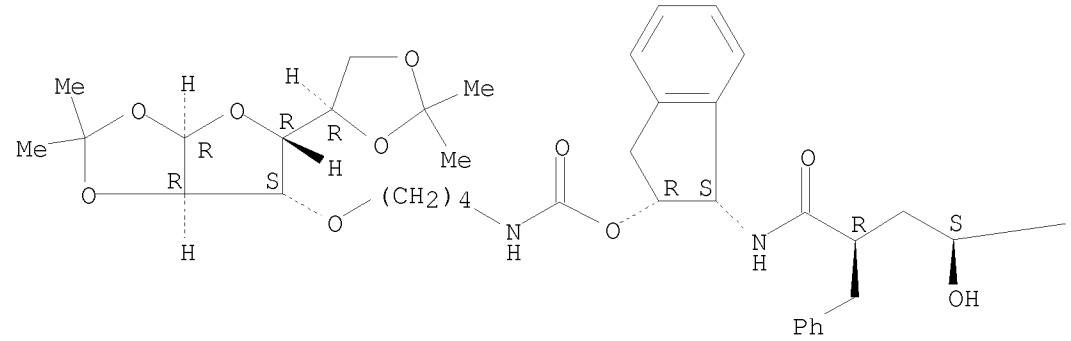


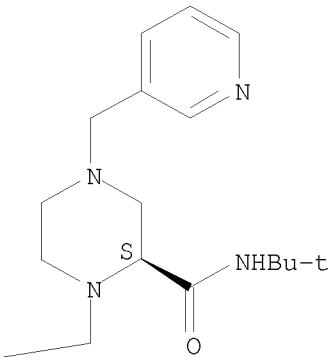
RN 404001-89-4 CAPLUS

CN α-D-Glucofuranose, 3-O-[4-[[[[(1S,2R)-2,3-dihydro-1-[[2,3,5-trideoxy-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)-D-erythro-pentonoyl]amino]-1H-inden-2-yl]oxy]carbonyl]amino]butyl]-1,2:5,6-bis-O-(1-methylethylidene)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



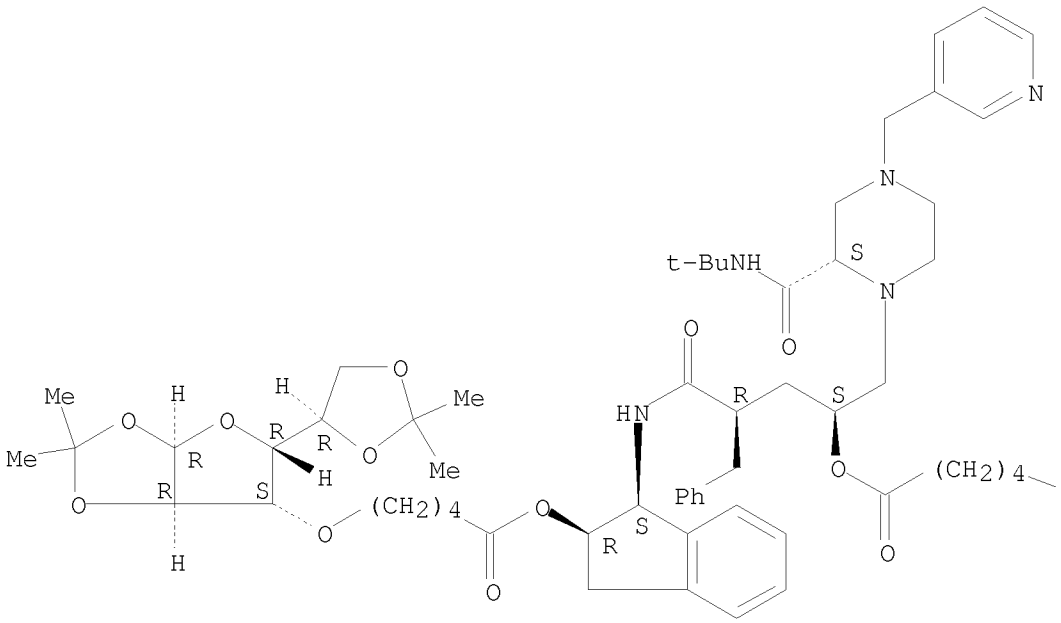


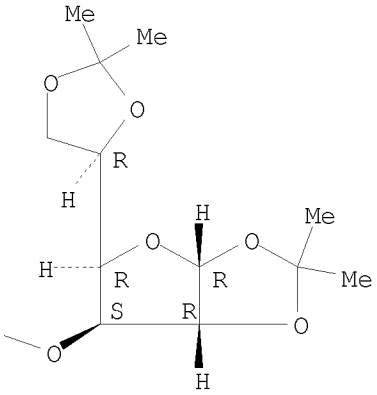
IT 404002-05-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis and anti-HIV activity of glucose-containing prodrugs derived from saquinavir, indinavir, and nelfinavir)

RN 404002-05-7 CAPLUS

CN α-D-Glucofuranose, 3-O-(4-carboxybutyl)-1,2:5,6-bis-O-(1-methylethylidene)-, ester with 3-O-[5-[[(1S,2R)-2,3-dihydro-1-[[2,3,5-trideoxy-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)-D-erythro-pentonoyl]amino]-1H-inden-2-yl]oxy]-5-oxopentyl]-1,2:5,6-bis-O-(1-methylethylidene)-α-D-glucofuranose (9CI) (CA INDEX NAME)

Absolute stereochemistry.





RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

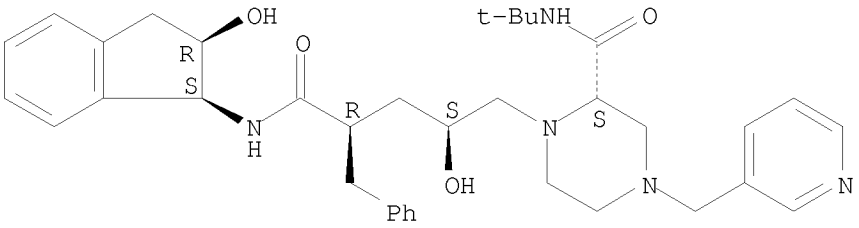
L8 ANSWER 2 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2001:678583 CAPLUS
DN 136:48003
TI Peptide mimetic HIV protease inhibitors are ligands for the orphan receptor SXR
AU Dussault, Isabelle; Lin, Min; Hollister, Kevin; Wang, Eric H.; Synold, Timothy W.; Forman, Barry Marc
CS Division of Molecular Medicine, The Gonda Diabetes and Genetic Research Center, Beckman Research Institute, City of Hope National Medical Center, Duarte, CA, 91010, USA
SO Journal of Biological Chemistry (2001), 276(36), 33309-33312
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB The orphan nuclear receptor SXR coordinately regulates drug clearance in response to a wide variety of xenobiotic compds. This signaling system protects the body from exposure to toxic compds.; however, it can also pose a severe barrier to drug therapy. We now demonstrate that the human immunodeficiency virus (HIV) protease inhibitor ritonavir binds SXR and activates its target genes. This represents an example of a commonly used therapeutic agent that effectively activates SXR. We also show that other protease inhibitors are weaker (saquinavir) or unable to activate SXR (nelfinavir, indinavir) thus defining analogs that fail to induce SXR-regulated clearance pathways. Interestingly, HIV protease inhibitors are distinct from previously known SXR ligands in that they are peptide mimetic compds. This expands the ligand specificity of SXR to include this unique chemical class whose pharmaceutical significance is expanding. Finally, we show that SXR ligands activate expression of multiple resistance protein 2 (MRP2), a critical regulator of bile flow and biliary drug excretion. These findings have important implications for the role of SXR in regulating drug clearance and hepatic disorders associated with impaired bile flow.
IT 150378-17-9, Indinavir
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(peptide mimetic HIV proteinase inhibitors are ligands for the orphan receptor SXR)

RN 150378-17-9 CAPLUS

CN D-erythro-Pentonamide, 2,3,5-trideoxy-N-[(1S,2R)-2,3-dihydro-2-hydroxy-1H-inden-1-yl]-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2001:122158 CAPLUS

DN 134:311179

TI 3,8-Diazabicyclo[3.2.1]octan-2-one Peptide Mimetics: Synthesis of a Conformationally Restricted Inhibitor of Farnesyltransferase

AU Dinsmore, Christopher J.; Bergman, Jeffrey M.; Bogusky, Michael J.; Culberson, J. Christopher; Hamilton, Kelly A.; Graham, Samuel L.

CS Departments of Medicinal Chemistry Molecular Systems and Cancer Research, Merck Research Laboratories, West Point, PA, 19486, USA

SO Organic Letters (2001), 3(6), 865-868
CODEN: ORLEF7; ISSN: 1523-7060

PB American Chemical Society

DT Journal

LA English

OS CASREACT 134:311179

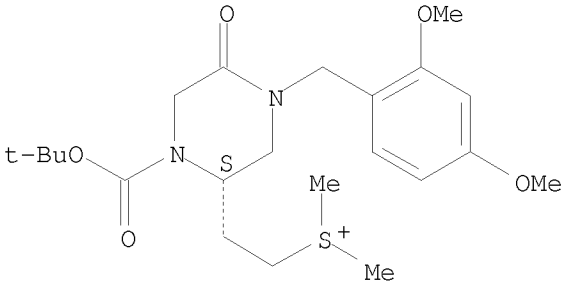
AB A new synthesis of the 3,8-diazabicyclo[3.2.1]octan-2-one framework is described. Transannular enolate alkylation of piperazinone derivs. provides a flexible route to highly constrained bicyclic peptidomimetic synthons with substitution at the Cα position. The chemical was used to produce a conformationally constrained farnesyltransferase inhibitor, which aided the elucidation of enzyme-bound conformation.

IT 335160-88-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of a conformationally restricted farnesyltransferase inhibitor based on 3,8-diazabicyclo[3.2.1]octanone)

RN 335160-88-8 CAPLUS

CN Sulfonium, [2-[(2S)-4-[(2,4-dimethoxyphenyl)methyl]-1-[(1,1-dimethylethoxy)carbonyl]-5-oxo-2-piperazinyl]ethyl]dimethyl-, iodide (9CI) (CA INDEX NAME)

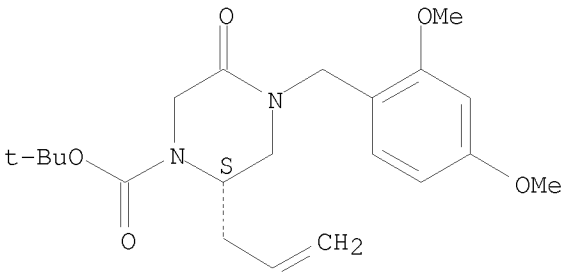
Absolute stereochemistry.



IT 335160-65-1P 335160-67-3P 335160-69-5P
335160-71-9P 335160-75-3P 335160-77-5P
335160-79-7P 335160-81-1P 335160-86-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of a conformationally restricted farnesyltransferase inhibitor based on 3,8-diazabicyclo[3.2.1]octanone)

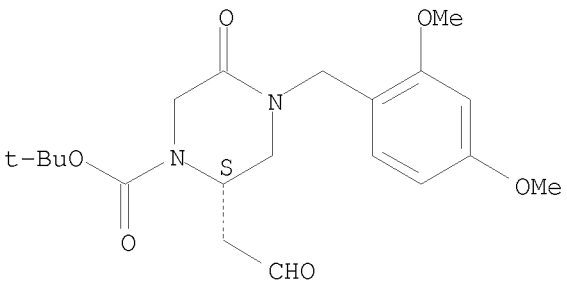
RN 335160-65-1 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[(2,4-dimethoxyphenyl)methyl]-5-oxo-2-(2-propenyl)-, 1,1-dimethylethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 335160-67-3 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[(2,4-dimethoxyphenyl)methyl]-5-oxo-2-(2-oxoethyl)-, 1,1-dimethylethyl ester, (2S)- (CA INDEX NAME)

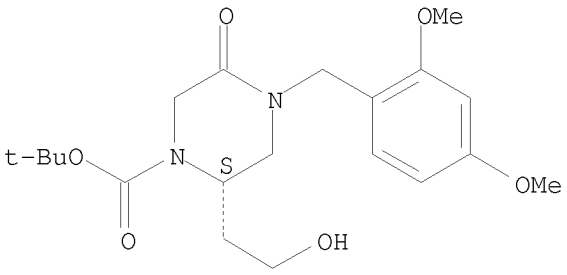
Absolute stereochemistry.



RN 335160-69-5 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[(2,4-dimethoxyphenyl)methyl]-2-(2-

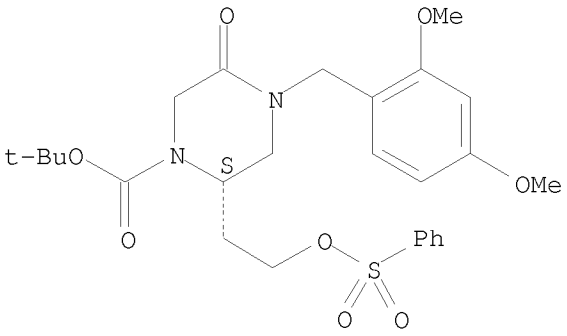
hydroxyethyl)-5-oxo-, 1,1-dimethylethyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



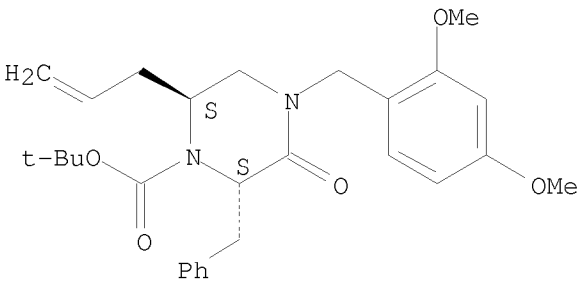
RN 335160-71-9 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[(2,4-dimethoxyphenyl)methyl]-5-oxo-2-[2-[(phenylsulfonyl)oxy]ethyl]-, 1,1-dimethylethyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



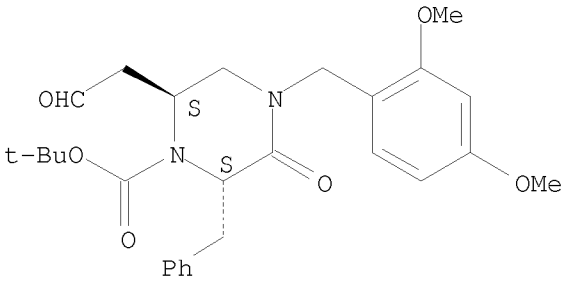
RN 335160-75-3 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[(2,4-dimethoxyphenyl)methyl]-3-oxo-2-(phenylmethyl)-6-(2-propenyl)-, 1,1-dimethylethyl ester, (2S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



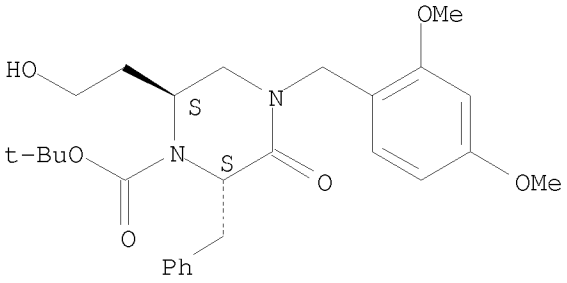
RN 335160-77-5 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[(2,4-dimethoxyphenyl)methyl]-3-oxo-6-(2-oxoethyl)-2-(phenylmethyl)-, 1,1-dimethylethyl ester, (2S,6S)- (CA INDEX NAME)

Absolute stereochemistry.



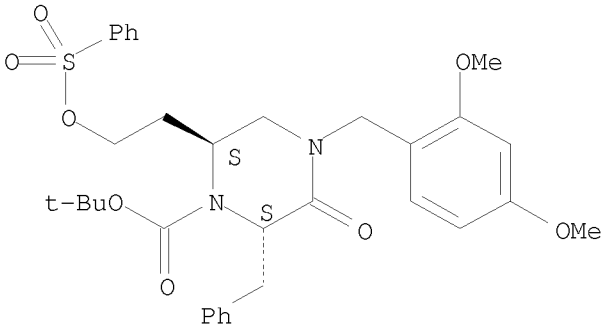
RN 335160-79-7 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[(2,4-dimethoxyphenyl)methyl]-6-(2-hydroxyethyl)-3-oxo-2-(phenylmethyl)-, 1,1-dimethylethyl ester, (2S,6S)- (CA INDEX NAME)

Absolute stereochemistry.



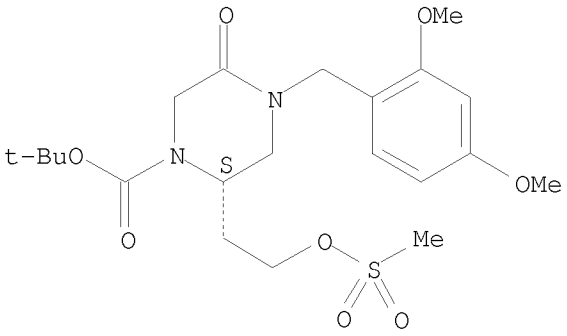
RN 335160-81-1 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[(2,4-dimethoxyphenyl)methyl]-3-oxo-2-(phenylmethyl)-6-[2-[(phenylsulfonyl)oxy]ethyl]-, 1,1-dimethylethyl ester, (2S,6S)- (CA INDEX NAME)

Absolute stereochemistry.



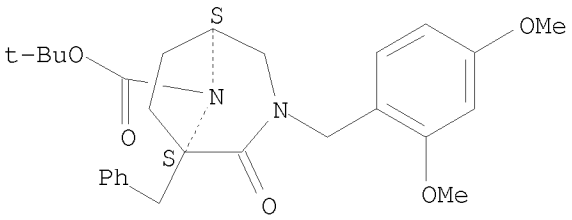
RN 335160-86-6 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[(2,4-dimethoxyphenyl)methyl]-2-[2-[(methylsulfonyl)oxy]ethyl]-5-oxo-, 1,1-dimethylethyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



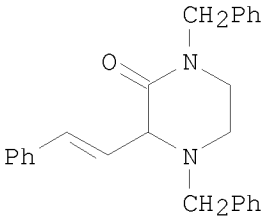
IT 335160-83-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of a conformationally restricted farnesyltransferase inhibitor based on 3,8-diazabicyclo[3.2.1]octanone)
RN 335160-83-3 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane-8-carboxylic acid, 3-[(2,4-dimethoxyphenyl)methyl]-2-oxo-1-(phenylmethyl)-, 1,1-dimethylethyl ester, (1S,5S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

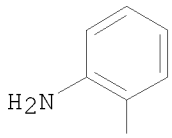


RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

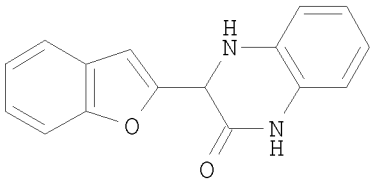
L8 ANSWER 4 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2000:897532 CAPLUS
DN 134:147573
TI Synthesis of piperazinones and benzopiperazinones from 1,2-diamines and organoboronic acids
AU Petasis, N. A.; Patel, Z. D.
CS Department of Chemistry and Loker Hydrocarbon Research Institute, University of Southern California, Los Angeles, CA, 90089-1661, USA
SO Tetrahedron Letters (2000), 41(49), 9607-9611
CODEN: TELEAY; ISSN: 0040-4039
PB Elsevier Science Ltd.
DT Journal
LA English
OS CASREACT 134:147573
GI



I



II



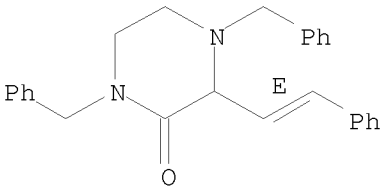
III

AB Alkenyl, aryl and heteroaryl boronic acids, e.g. PhCH:CHB(OH)2, react with 1,2-diamines, e.g. PhCH2NHCH2CH2NHCH2Ph, and glyoxylic acid to give directly in one step the corresponding piperazinones, e.g. I. Similarly, the use of monoprotected 1,2-phenylenediamine, e.g. II, leads to benzopiperazinones, e.g. III.

IT 324524-49-4P 324524-51-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of piperazinones and benzopiperazinones via cyclization of boronic acids with diamines and glyoxylic acid)

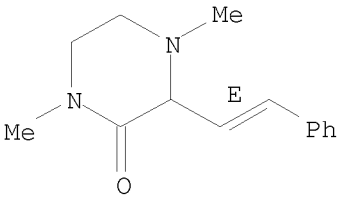
RN 324524-49-4 CAPLUS
CN Piperazinone, 3-[(1E)-2-phenylethenyl]-1,4-bis(phenylmethyl)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



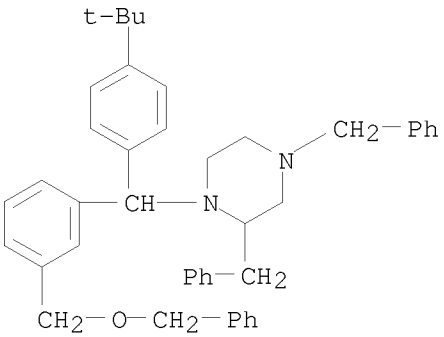
RN 324524-51-8 CAPLUS
CN Piperazinone, 1,4-dimethyl-3-[(1E)-2-phenylethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2000:894543 CAPLUS
DN 135:71099
TI The fine tuning of high affinity and selective non-peptide agonists of the δ-opioid receptor via solution and solid-phase
AU Alfaro-Lopez, Josue; Okayama, Toru; Hosohata, Keiko; Davis, Peg; Porreca, Frank; Yamamura, Henry I.; Hruby, Victor J.
CS Department of Chemistry, The University of Arizona, Tucson, AZ, 85721, USA
SO Peptides for the New Millennium, Proceedings of the American Peptide Symposium, 16th, Minneapolis, MN, United States, June 26-July 1, 1999 (2000), Meeting Date 1999, 38-39. Editor(s): Fields, Gregg B.; Tam, James P.; Barany, George. Publisher: Kluwer Academic Publishers, Dordrecht, Neth.
CODEN: 69ATHX
DT Conference
LA English
AB A systematic approach to peptide and peptidomimetic design has been presented by Hruby et al. (Ann. N.Y. Acad. Sci., p. 7, volume 757, 1995). By applying this scheme to an ongoing research which seeks to translate the information contained in an endogenous opioid peptide such as enkephalin into a small organic compound, a series of new peptidomimetic compds. has been reported. The design was based on the topog. constrained and highly selective peptide [(2S,3R)TMT]DPDPE. SL-3111 (I) emerged as a promising non-peptidomimetic lead for further design, showing 8 nM binding affinity and over 2000-fold selectivity for bioassays, in spite of having a moderate selectivity of 460-fold μ/δ, it showed low potency. Efforts to improve the biol. profile of SL-3111, through the design and synthesis of a second generation of peptidomimetics, are reported.
IT 346467-74-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(selective non-peptide δ-opioid receptor agonists design)
RN 346467-74-1 CAPLUS
CN Piperazine, 1-[[4-(1,1-dimethylethyl)phenyl][3-[(phenylmethoxy)methyl]phenyl]methyl]-2,4-bis(phenylmethyl)- (CA INDEX NAME)



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2000:812639 CAPLUS
DN 134:71891

TI Synthesis of chiral piperazinones as versatile scaffolds for peptidomimetics

AU Rubsam, Frank; Mazitschek, Ralph; Giannis, Athanassios
CS Institut fur Organische Chemie der Universitat Karlsruhe, Karlsruhe, D-76128, Germany

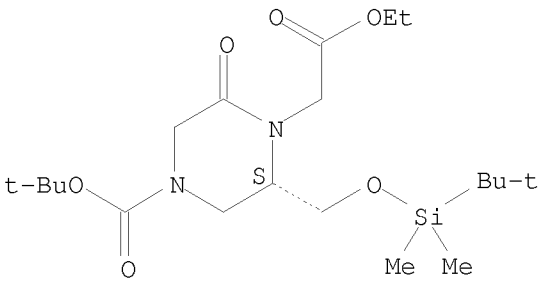
SO Tetrahedron (2000), 56(43), 8481-8487
CODEN: TETRAB; ISSN: 0040-4020
PB Elsevier Science Ltd.
DT Journal
LA English
OS CASREACT 134:71891

AB Chiral piperazinones were synthesized as conformationally restricted peptidomimetics via reductive amination starting from inexpensive and readily available D-glucosamine hydrochloride and amino acid Me esters. Different synthetic strategies are devised to allow attachment of side chains imitating the parent peptide as shown for the RGD motif.

IT 315229-45-9P 315229-46-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of chiral piperazinones as peptidomimetics of RGD peptide motif)

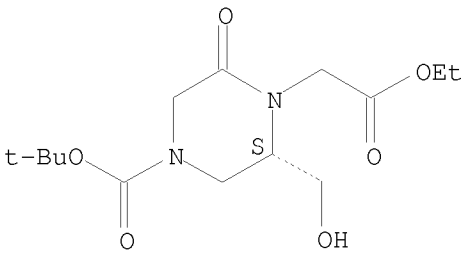
RN 315229-45-9 CAPLUS
CN 1-Piperazineacetic acid, 4-[(1,1-dimethylethoxy)carbonyl]-2-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-6-oxo-, ethyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 315229-46-0 CAPLUS
CN 1-Piperazineacetic acid, 4-[(1,1-dimethylethoxy)carbonyl]-2-(hydroxymethyl)-6-oxo-, ethyl ester, (2S)- (CA INDEX NAME)

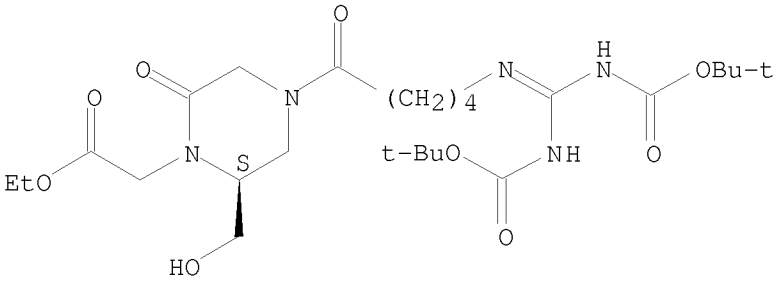
Absolute stereochemistry. Rotation (+).



IT 315229-48-2P 315229-49-3P 315229-50-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of chiral piperazinones as peptidomimetics of RGD peptide motif)

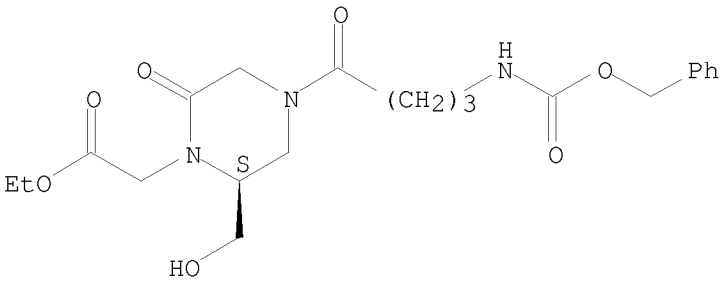
RN 315229-48-2 CAPLUS
CN 1-Piperazineacetic acid, 4-[5-[[bis[[(1,1-dimethylethoxy)carbonyl]amino]methylene]amino]-1-oxopentyl]-2-(hydroxymethyl)-6-oxo-, ethyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



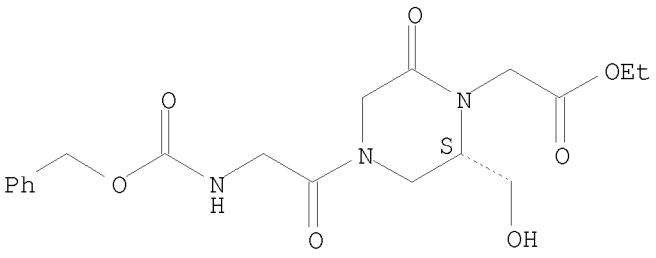
RN 315229-49-3 CAPLUS
CN 1-Piperazineacetic acid, 2-(hydroxymethyl)-6-oxo-4-[1-oxo-4-[[(phenylmethoxy)carbonyl]amino]butyl]-, ethyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 315229-50-6 CAPLUS
CN 1-Piperazineacetic acid, 2-(hydroxymethyl)-6-oxo-4-[[[(phenylmethoxy)carbonyl]amino]acetyl]-, ethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

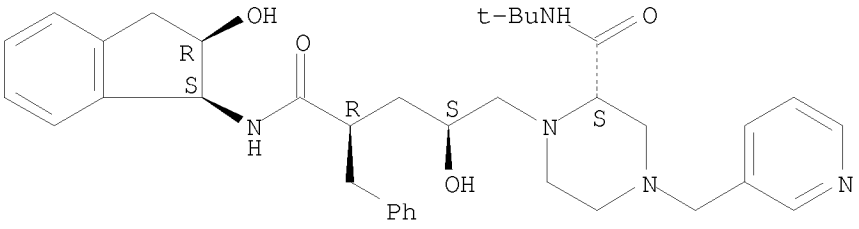


RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2000:708749 CAPLUS
DN 134:202449

TI Tipranavir inhibits broadly protease inhibitor-resistant HIV-1 clinical samples
AU Larder, Brendan A.; Hertogs, Kurt; Bloor, Stuart; van den Eynde, Ch.; DeCian, Wanda; Wang, Yenyun; Freimuth, William W.; Tarpley, Gary
CS Virco UK Ltd, Cambridge, UK
SO AIDS (London) (2000), 14(13), 1943-1948
CODEN: AIDSET; ISSN: 0269-9370
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB The antiviral activity of tipranavir (TPV), a nonpeptide HIV-1 protease inhibitor (PI), was assessed in vitro on 134 clin. isolates with a wide range of resistance to currently available peptidomimetic PI. The susceptibility of all 134 variants was then retested simultaneously with 4 PI (indinavir, ritonavir, nelfinavir, saquinavir) plus TPV, using the Antivirogram assay. Of 105 viruses with >10-fold resistance to three of the 4 PI and an average of 6.1 PI mutations per sample, 95 (90%) were susceptible to TPV; 8 (8%) had 4-10-fold resistance to TPV and only 2 (2%) had >10-fold resistance. The substantial lack of PI cross-resistance to TPV shown by highly PI-resistant clin. isolates makes TPV an attractive new-generation HIV inhibitor.
IT 150378-17-9, Indinavir
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(tipranavir inhibition of HIV-1 resistant to)
RN 150378-17-9 CAPLUS
CN D-erythro-Pentonamide, 2,3,5-trideoxy-N-[(1S,2R)-2,3-dihydro-2-hydroxy-1H-inden-1-yl]-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

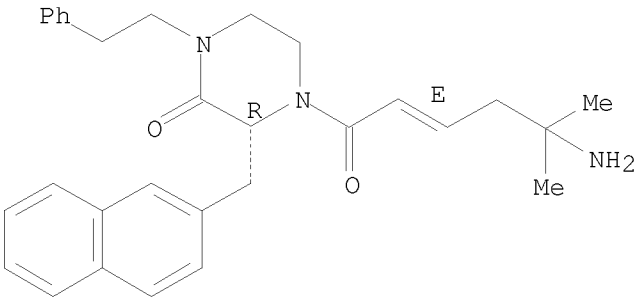
L8 ANSWER 8 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2000:535988 CAPLUS
DN 133:267133
TI New highly potent dipeptidic growth hormone secretagogues with low molecular weight
AU Peschke, Bernd; Ankersen, Michael; Hansen, Thomas Kruse; Hansen, Birgit Sehested; Lau, Jesper; Nielsen, Karin Kramer; Raun, Kirsten
CS Health Care Chemistry, Novo Nordisk A/S, Malov, 2760, Den.
SO European Journal of Medicinal Chemistry (2000), 35(6), 599-618
CODEN: EJMCA5; ISSN: 0223-5234
PB Editions Scientifiques et Medicales Elsevier
DT Journal
LA English
AB Based on NN703, low mol. weight growth hormone secretagogues (GHSs) with a reduced number of hydrogen binding sites were designed by removal of the C-terminal amide group. The compds. were highly potent in combination with high efficacy in a rat pituitary cell assay, being characterized with

EC50 values down to 0.8 nM. Selected compds. were tested in in vivo animal models. The oral bioavailability in dogs was 16-44%. Also, the ED50 values of the compds. were determined both in dog and swine.

IT 202810-68-2P 297175-39-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and biol. activity of highly potent dipeptidic growth hormone secretagogues with low mol. wts.)

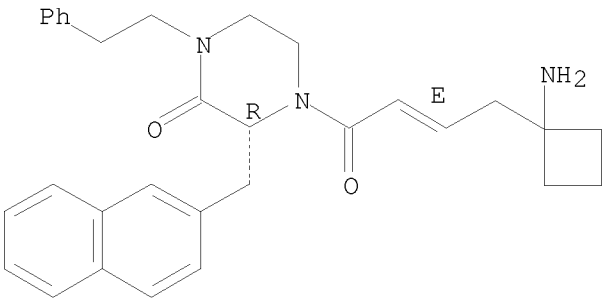
RN 202810-68-2 CAPLUS
CN Piperazinone, 4-[(2E)-5-amino-5-methyl-1-oxo-2-hexenyl]-3-(2-naphthalenylmethyl)-1-(2-phenylethyl)-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 297175-39-4 CAPLUS
CN Piperazinone, 4-[(2E)-4-(1-aminocyclobutyl)-1-oxo-2-butenyl]-3-(2-naphthalenylmethyl)-1-(2-phenylethyl)-, (3R)- (9CI) (CA INDEX NAME)

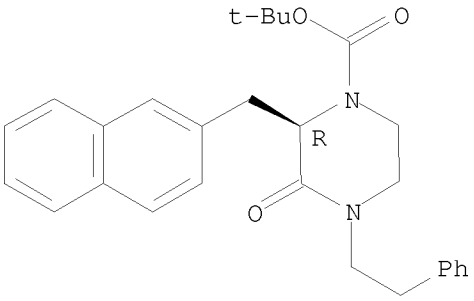
Absolute stereochemistry.
Double bond geometry as shown.



IT 202811-56-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and biol. activity of highly potent dipeptidic growth hormone secretagogues with low mol. wts.)

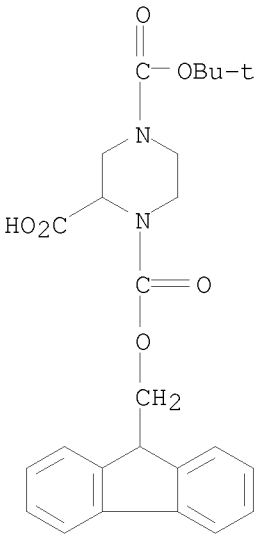
RN 202811-56-1 CAPLUS
CN 1-Piperazinecarboxylic acid, 2-(2-naphthalenylmethyl)-3-oxo-4-(2-phenylethyl)-, 1,1-dimethylethyl ester, (2R)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2000:443462 CAPLUS
DN 133:223022
TI Solid supported high-throughput organic synthesis of peptide β-turn mimetics via tandem Petasis reaction/diketopiperazine formation
AU Golebiowski, A.; Klopfenstein, S. R.; Chen, J. J.; Shao, X.
CS Health Care Research Center, Combinatorial Chemistry Group, Procter & Gamble Pharmaceuticals, Mason, OH, 45040-8006, USA
SO Tetrahedron Letters (2000), 41(25), 4841-4844
CODEN: TELEAY; ISSN: 0040-4039
PB Elsevier Science Ltd.
DT Journal
LA English
OS CASREACT 133:223022
AB High-throughput organic synthesis of bicyclic diketopiperazines, β-turn mimetics, is described. Starting from Merrifield resin-bound piperazine-2-carboxylate, first two side-chains are introduced via the Petasis reaction and subsequent amide bond formation. Unblocking the α-amino group of piperazine-2-carboxylate, Boc-N-protected α-amino acid coupling, and deprotection followed by cyclative cleavage introduces the remaining side-chains.
IT 183742-23-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(solid-phase high-throughput synthesis of peptide β-turn mimetics via tandem Petasis reaction/diketopiperazine formation)
RN 183742-23-6 CAPLUS
CN 1,2,4-Piperazinetricarboxylic acid, 4-(1,1-dimethylethyl) 1-(9H-fluoren-9-ylmethyl) ester (CA INDEX NAME)



RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2000:311662 CAPLUS
DN 133:114640
TI Synthesis and anti-HIV activity of prodrugs derived from saquinavir and indinavir
AU Giorgio, Audrey Farese-Di; Rouquayrol, Marielle; Greiner, Jacques; Aubertin, Anne-Marie; Vierling, Pierre; Guedj, Roger
CS Laboratoire de Chimie Bio-Organique, ESA 6001 CNRS, Universite de Nice Sophia-Antipolis, Nice, 06108, Fr.
SO Antiviral Chemistry & Chemotherapy (2000), 11(2), 97-110
CODEN: ACCHEH; ISSN: 0956-3202
PB International Medical Press
DT Journal
LA English
AB With a view to improving the pharmacol. properties, safety and pharmacokinetic profiles of current protease inhibitors, the synthesis of various acyl-substituted saquinavir and indinavir prodrugs, their in vitro stability with respect to hydrolysis and their anti-HIV (LAI and HTLV IIIB) activity and cytotoxicity in CEM-SS and MT4 cells have been investigated. Hydrolysis of the ester bond and liberation of the active free drug was crucial for HIV inhibition: the faster the hydrolysis, the closer the anti-HIV activity was to that of the resp. parent drug. This is the case for most of the C-14-substituted indinavir and saquinavir derivs. (IC50 from 10 to 360 nM for ester half-lives of 90 min to 40 h). Concomitantly, the level of HIV inhibition is very low for the prodrugs for which hydrolysis is very slow. This is the case with the myristoyl or oleyl saquinavir esters, owing to the stable masking of the hydroxyl that is part of the peptidomimetic non-cleavable transition state isostere responsible for the inhibitory potency of saquinavir (and indinavir). In contrast, the anti-HIV activity of the monosubstituted C-8 indinavir prodrugs seems not to be correlated with their resistance to hydrolysis, as expected (the C-8 hydroxyl of indinavir is not involved in the transition state isostere). No cytotoxicity was detected for the indinavir and saquinavir prodrugs for concns. as high as 10 or even 100 μM, thus indicating promising therapeutic potential.
IT 157810-81-6, Indinavir sulfate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); BIOL (Biological study)
(preparation and anti-HIV activity of prodrugs derived from saquinavir and indinavir)

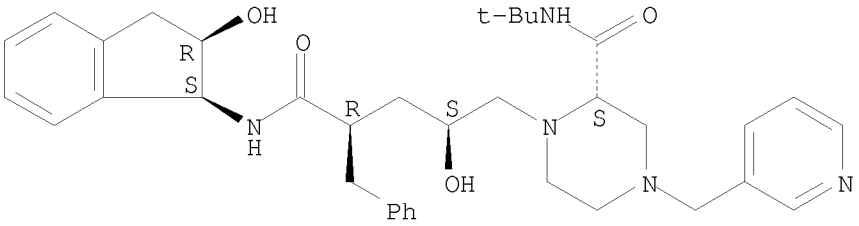
RN 157810-81-6 CAPLUS

CN D-erythro-Pentonamide, 2,3,5-trideoxy-N-[(1S,2R)-2,3-dihydro-2-hydroxy-1H-inden-1-yl]-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)-, sulfate (1:1) (CA INDEX NAME)

CM 1

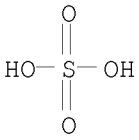
CRN 150378-17-9
CMF C36 H47 N5 O4

Absolute stereochemistry.



CM 2

CRN 7664-93-9
CMF H2 O4 S

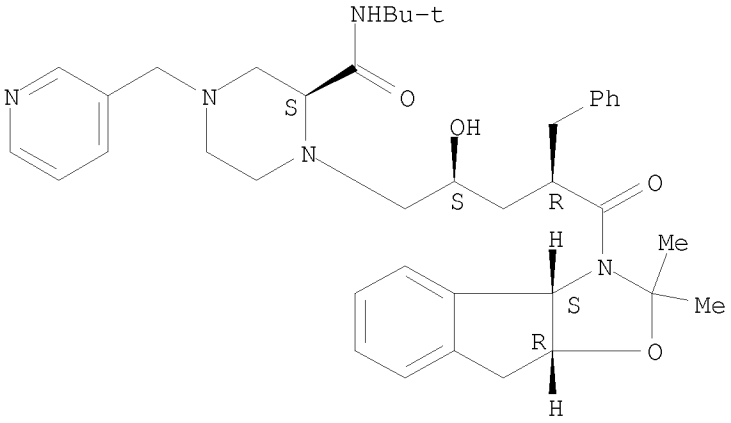


IT 185213-44-9P 244614-35-5P 244614-36-6P
244614-38-8P 244614-39-9P 244614-42-4P
285991-80-2P 285991-81-3P 285991-82-4P
285991-83-5P 285991-84-6P 285991-86-8P
285991-87-9P 285991-89-1P 285991-91-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and anti-HIV activity of prodrugs derived from saquinavir and indinavir)

RN 185213-44-9 CAPLUS

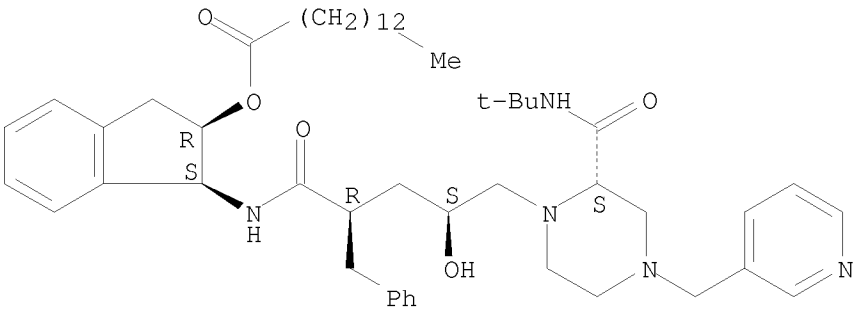
CN 2H-Indeno[1,2-d]oxazole, 3,3a,8,8a-tetrahydro-2,2-dimethyl-3-[2,3,5-trideoxy-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)-D-erythro-pentonoyl]-, (3aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



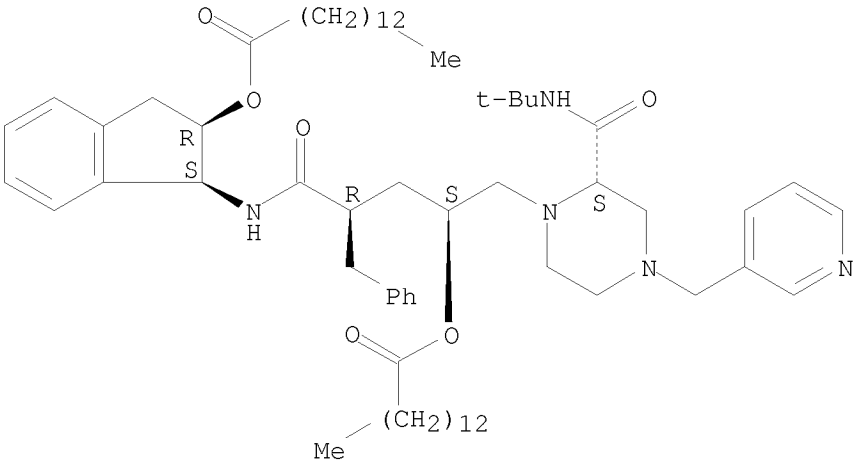
RN 244614-35-5 CAPLUS
CN D-erythro-Pentonamide, 2,3,5-trideoxy-N-[(1S,2R)-2,3-dihydro-2-[(1-oxotetradecyl)oxy]-1H-inden-1-yl]-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)- (CA INDEX NAME)

Absolute stereochemistry.

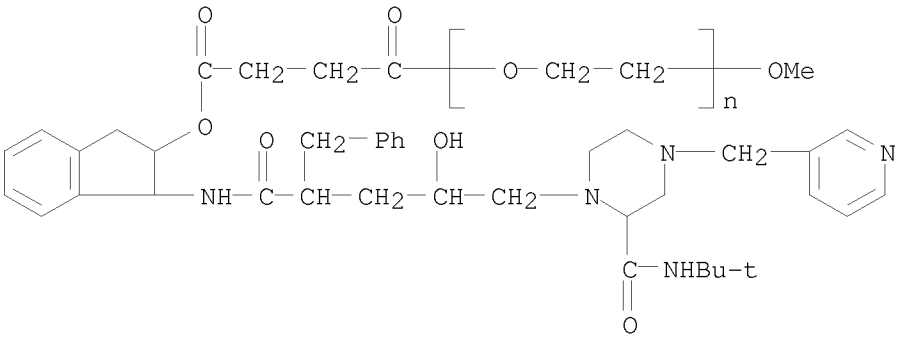


RN 244614-36-6 CAPLUS
CN D-erythro-Pentonamide, 2,3,5-trideoxy-N-[(1S,2R)-2,3-dihydro-2-[(1-oxotetradecyl)oxy]-1H-inden-1-yl]-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)-, 4-tetradecanoate (CA INDEX NAME)

Absolute stereochemistry.

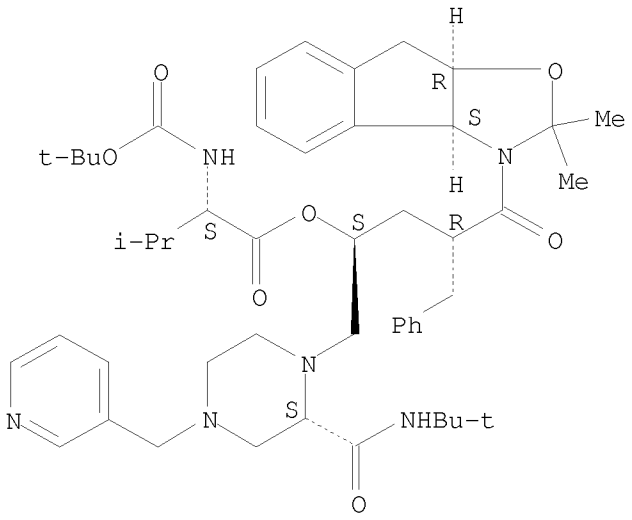


RN 244614-38-8 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[4-[[(1S,2R)-1-[[(2R,4S)-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-4-hydroxy-1-oxo-2-(phenylmethyl)pentyl]amino]-2,3-dihydro-1H-inden-2-yl]oxy]-1,4-dioxobutyl]-ω-methoxy- (9CI) (CA INDEX NAME)



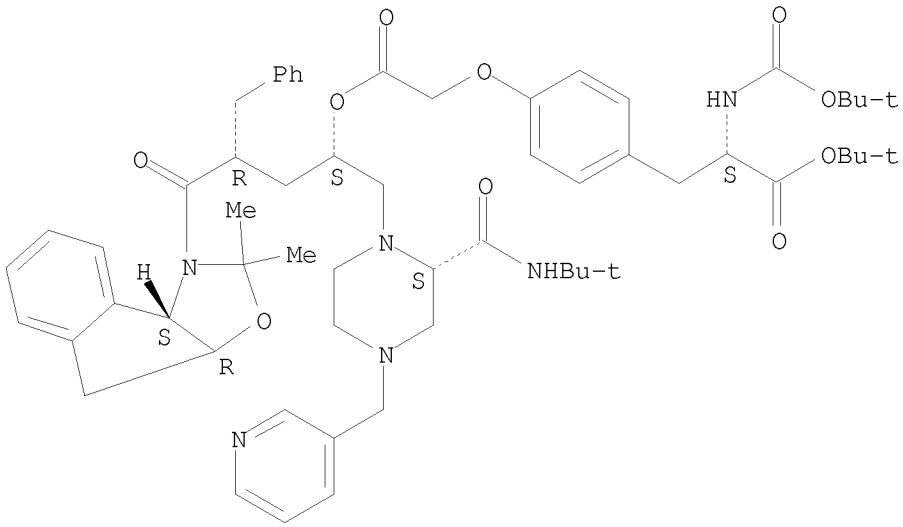
RN 244614-39-9 CAPLUS
CN L-Valine, N-[(1,1-dimethylethoxy)carbonyl]-, ester with (3aS,8aR)-3,3a,8,8a-tetrahydro-2,2-dimethyl-3-[2,3,5-trideoxy-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)-D-erythro-pentonoyl]-2H-indeno[1,2-d]oxazole (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 244614-42-4 CAPLUS
CN 2H-Indeno[1,2-d]oxazole, 3,3a,8,8a-tetrahydro-2,2-dimethyl-3-[2,3,5-trideoxy-4-O-[[4-[(2S)-3-(1,1-dimethylethoxy)-2-[[(1,1-dimethylethoxy)carbonyl]amino]-3-oxopropyl]phenoxy]acetyl]-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)-D-erythro-pentonoyl]-, (3aS,8aR)- (9CI) (CA INDEX NAME)

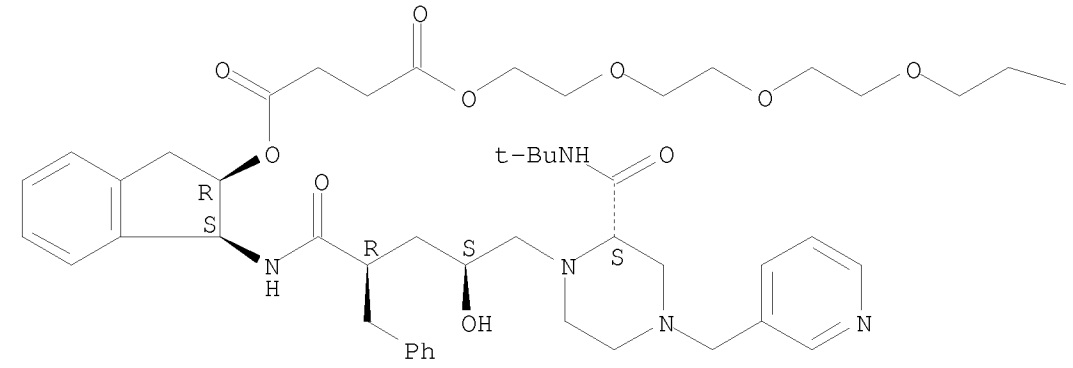
Absolute stereochemistry.



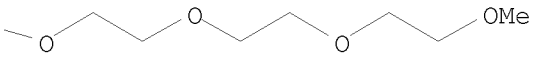
RN 285991-80-2 CAPLUS
CN D-erythro-Pentonamide, 2,3,5-trideoxy-N-[(1S,2R)-2,3-dihydro-2-[(1,4-dioxo-5,8,11,14,17,20,23,26-octaoxaheptacos-1-yl)oxy]-1H-inden-1-yl]-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



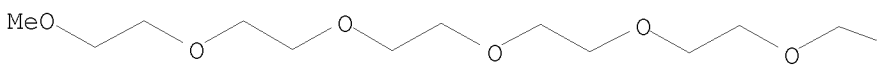
PAGE 1-B



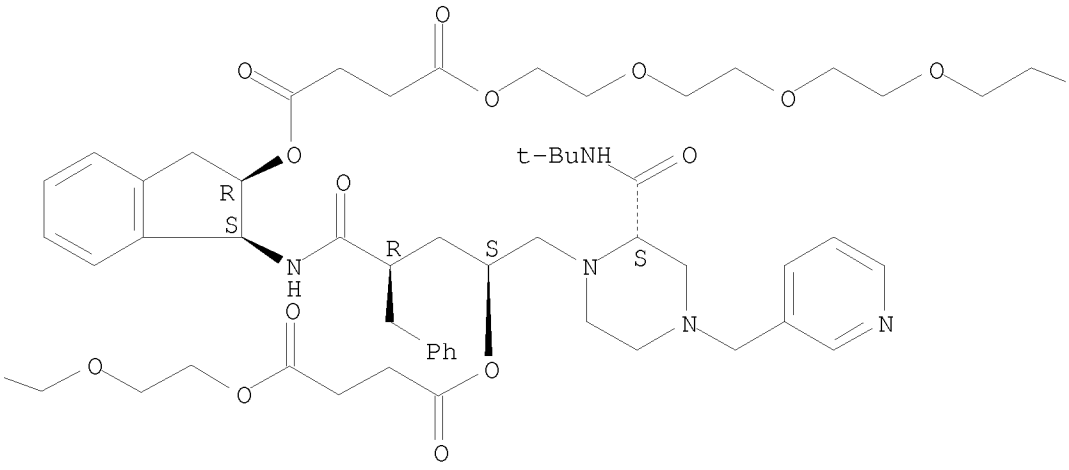
RN 285991-81-3 CAPLUS
CN D-erythro-Pentonamide, 2,3,5-trideoxy-N-[(1S,2R)-2,3-dihydro-2-[(1,4-dioxo-5,8,11,14,17,20,23,26-octaoxaheptacos-1-yl)oxy]-1H-inden-1-yl]-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)-, 4-(4-oxo-5,8,11,14,17,20,23,26-octaoxaheptacosanoate) (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

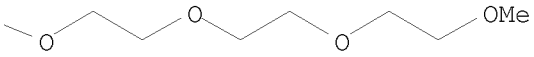
PAGE 1-A



PAGE 1-B

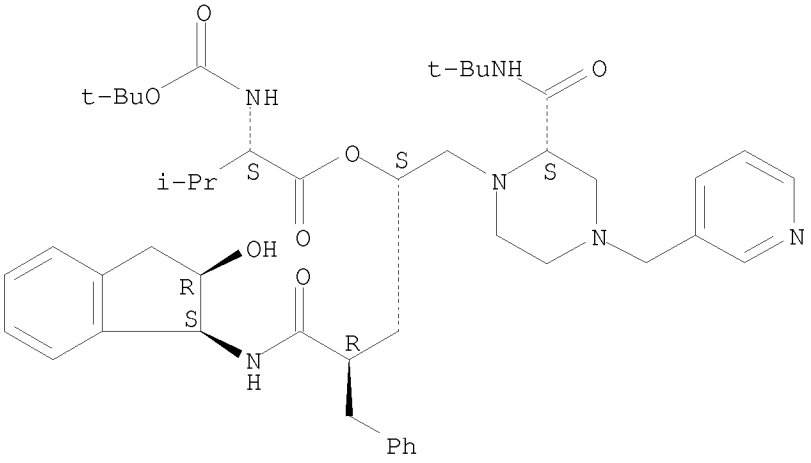


PAGE 1-C



RN 285991-82-4 CAPLUS
CN L-Valine, N-[(1,1-dimethylethoxy)carbonyl]-, 4-ester with 2,3,5-trideoxy-N-[(1S,2R)-2,3-dihydro-2-hydroxy-1H-inden-1-yl]-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)-D-erythro-pentonamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

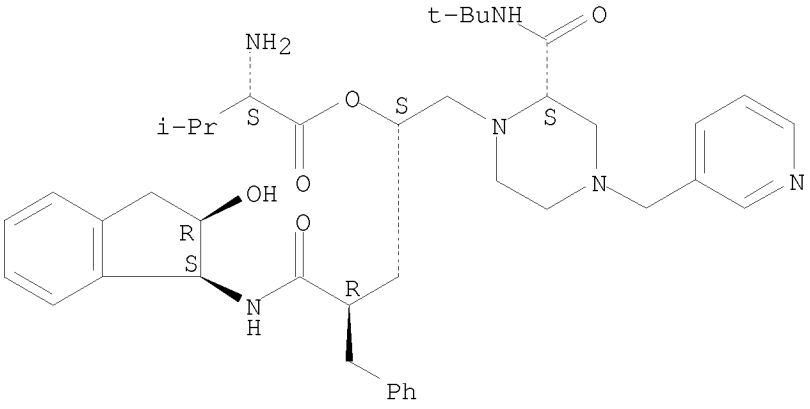


RN 285991-83-5 CAPLUS
CN L-Valine, 4-ester with 2,3,5-trideoxy-N-[(1S,2R)-2,3-dihydro-2-hydroxy-1H-inden-1-yl]-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)-D-erythro-pentonamide, tetrakis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

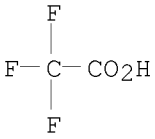
CRN 244614-40-2
CMF C41 H56 N6 O5

Absolute stereochemistry.



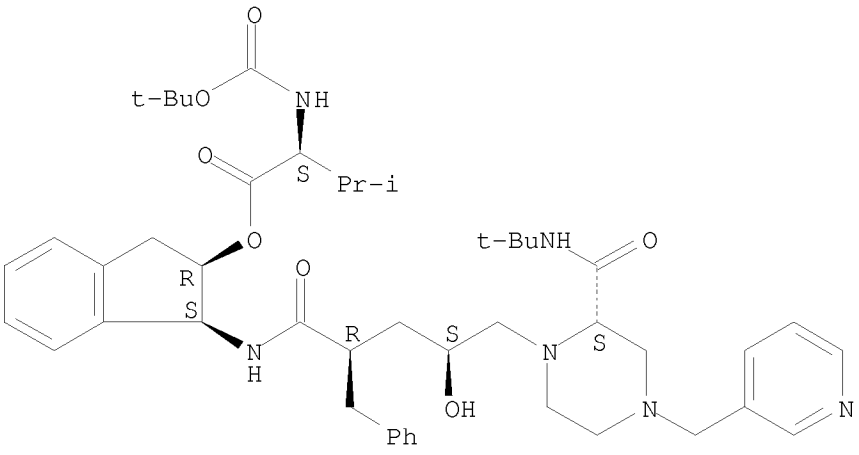
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 285991-84-6 CAPLUS
CN L-Valine, N-[(1,1-dimethylethoxy)carbonyl]-, (1S,2R)-2,3-dihydro-1-[[2,3,5-trideoxy-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)-D-erythro-pentonoyl]amino]-1H-inden-2-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

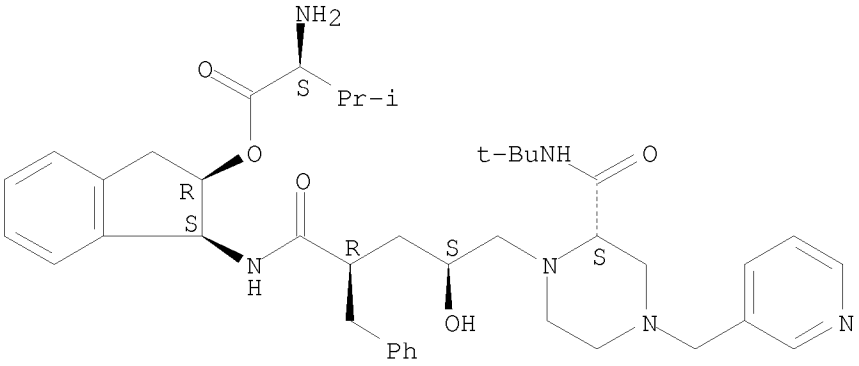


RN 285991-86-8 CAPLUS
CN L-Valine, (1S,2R)-2,3-dihydro-1-[[2,3,5-trideoxy-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)-D-erythro-pentonoyl]amino]-1H-inden-2-yl ester, tetrakis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

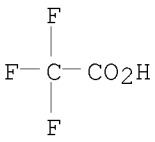
CRN 285991-85-7
CMF C41 H56 N6 O5

Absolute stereochemistry.



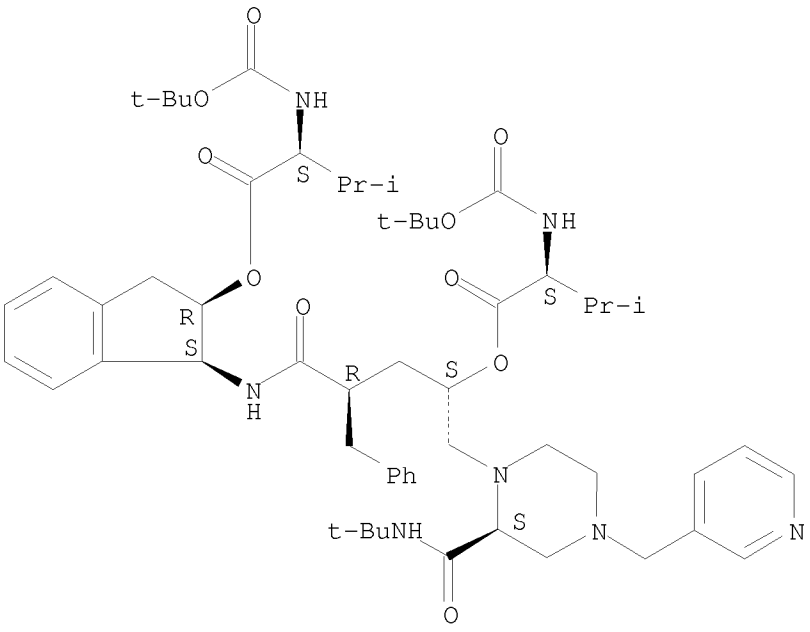
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 285991-87-9 CAPLUS
CN L-Valine, N-[(1,1-dimethylethoxy)carbonyl]-, (1S,2R)-2,3-dihydro-1-[[2,3,5-trideoxy-4-O-[(2S)-2-[[(1,1-dimethylethoxy)carbonyl]amino]-3-methyl-1-oxobutyl]-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)-D-erythro-pentonoyl]amino]-1H-inden-2-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

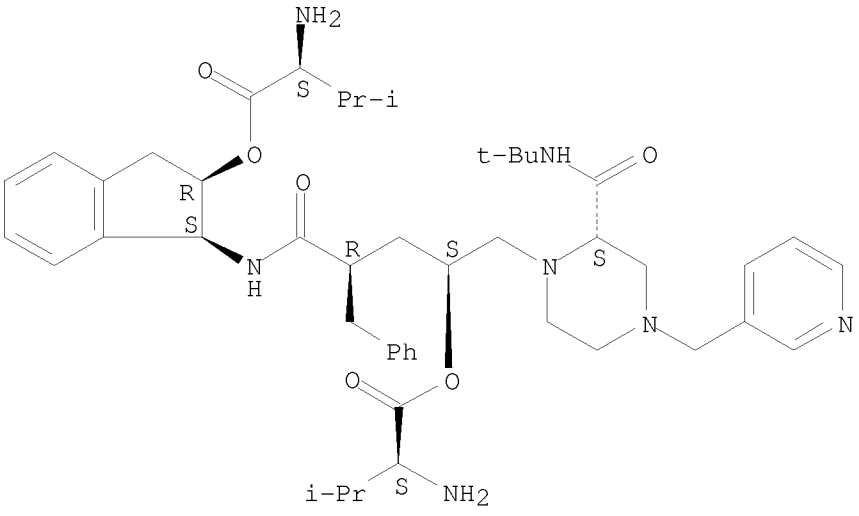


RN 285991-89-1 CAPLUS
CN L-Valine, (1S,2R)-1-[[4-O-[(2S)-2-amino-3-methyl-1-oxobutyl]-2,3,5-trideoxy-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)-D-erythro-pentonoyl]amino]-2,3-dihydro-1H-inden-2-yl ester, pentakis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

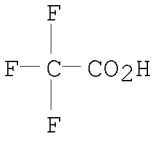
CRN 285991-88-0
CMF C46 H65 N7 O6

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

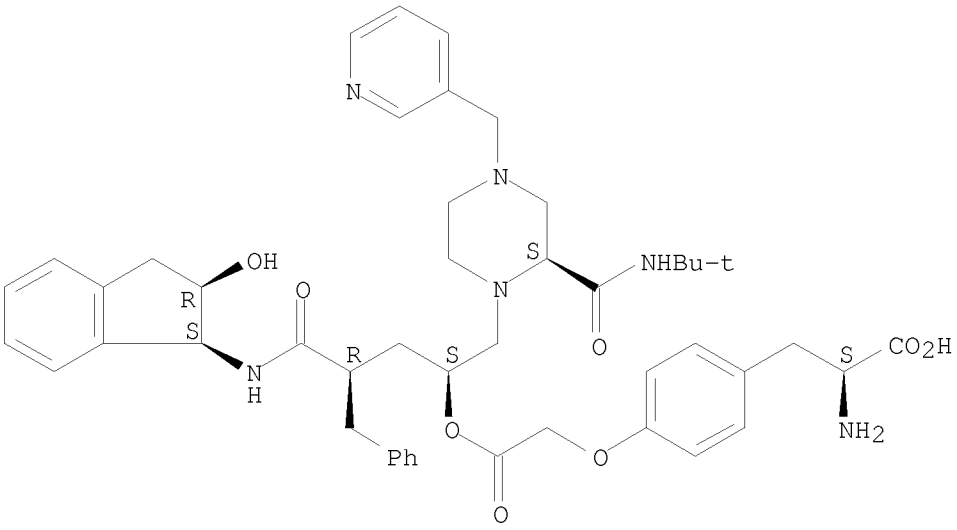


RN 285991-91-5 CAPLUS
CN D-erythro-Pentonamide, 2,3,5-trideoxy-N-[(1S,2R)-2,3-dihydro-2-hydroxy-1H-inden-1-yl]-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)-, 4-[[4-[(2S)-2-amino-2-carboxyethyl]phenoxy]acetate], tetrakis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

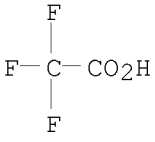
CRN 285991-90-4
CMF C47 H58 N6 O8

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



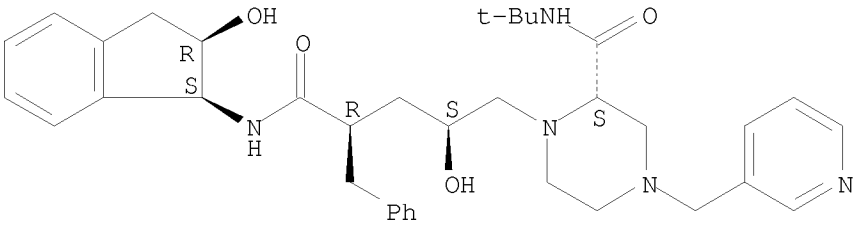
IT 150378-17-9, Indinavir
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation and anti-HIV activity of prodrugs derived from saquinavir and indinavir)

RN 150378-17-9 CAPLUS

CN D-erythro-Pentonamide, 2,3,5-trideoxy-N-[(1S,2R)-2,3-dihydro-2-hydroxy-1H-inden-1-yl]-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)- (CA INDEX NAME)

Absolute stereochemistry.



IT 285991-79-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

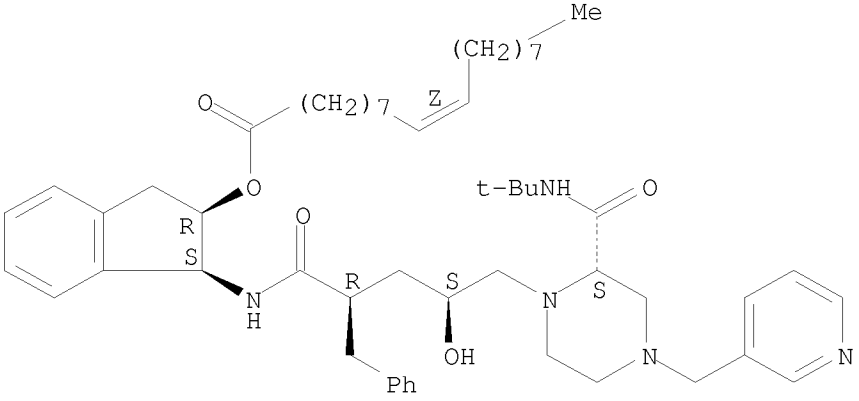
(preparation and anti-HIV activity of prodrugs derived from saquinavir and indinavir)

RN 285991-79-9 CAPLUS

CN D-erythro-Pentonamide, 2,3,5-trideoxy-N-[(1S,2R)-2,3-dihydro-2-[[(9Z)-1-oxo-9-octadecenyl]oxy]-1H-inden-1-yl]-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 11 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2000:296186 CAPLUS

DN 133:105336

TI Synthesis of a novel thyrotropin releasing hormone (TRH) analog incorporating a piperazin-2-one ring

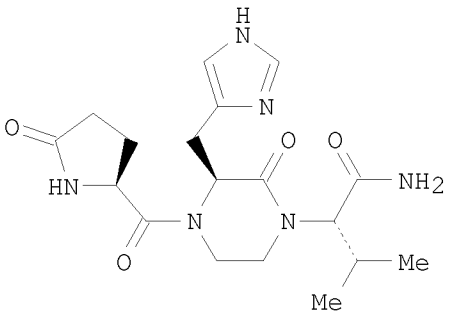
AU Bhatt, Ulhas; Just, George

CS Department of Chemistry, McGill University, Montreal, QC, H3A 2K6, Can.

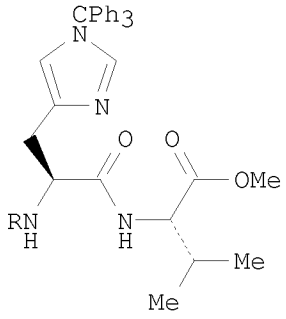
SO Helvetica Chimica Acta (2000), 83(4), 722-727
CODEN: HCACAV; ISSN: 0018-019X

PB Verlag Helvetica Chimica Acta

DT Journal
LA English
GI



I



II

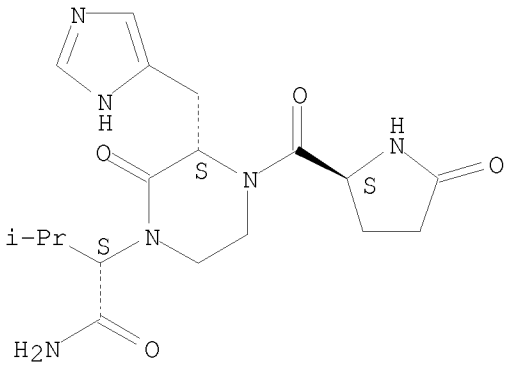
AB The synthesis of a TSH releasing hormone (TRH) analog, piperazinone-containing conformationally restricted peptidomimetic I, is described. The key recognition elements of the interaction between TRH and its receptor are retained in I. Synthesis of I started with dipeptide II (R = Fmoc) as the starting material, which was converted to its nitrobenzenesulfonylated derivative II (R = SO2C6H4NO2-4), followed by cyclization to the piperazinone derivative, N-acylation with L-pyroglutamate and deprotection to give I.

IT 282529-03-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of a piperazinone-containing peptidomimetic analog of TSH releasing hormone)

RN 282529-03-7 CAPLUS

CN 1-Piperazineacetamide, 3-(1H-imidazol-4-ylmethyl)-α-(1-methylethyl)-2-oxo-4-[[(2S)-5-oxo-2-pyrrolidinyl]carbonyl]-, (αS,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



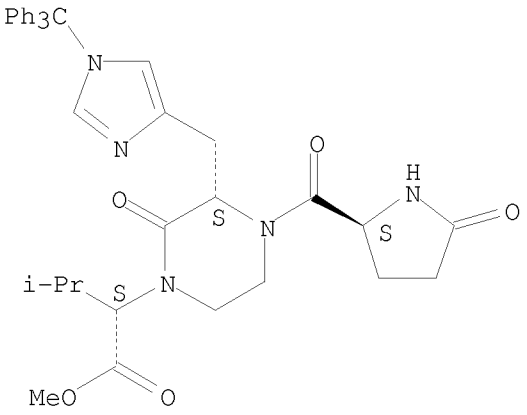
IT 282529-12-8P 282529-13-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of a piperazinone-containing peptidomimetic analog of TSH releasing hormone)

RN 282529-12-8 CAPLUS

CN 1-Piperazineacetic acid, α-(1-methylethyl)-2-oxo-4-[[(2S)-5-oxo-2-pyrrolidinyl]carbonyl]-3-[[1-(triphenylmethyl)-1H-imidazol-4-yl]methyl]-,

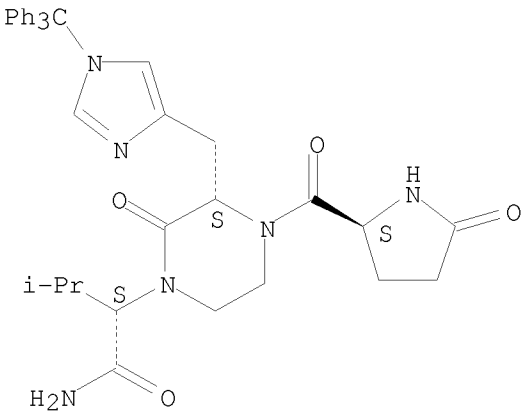
methyl ester, (αS,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 282529-13-9 CAPLUS
CN 1-Piperazineacetamide, α-(1-methylethyl)-2-oxo-4-[[(2S)-5-oxo-2-pyrrolidinyl]carbonyl]-3-[[1-(triphenylmethyl)-1H-imidazol-4-yl]methyl]-, (αS,3S)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 12 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2000:276168 CAPLUS
DN 133:53224
TI Comparison of human immunodeficiency virus type 1 Pr55Gag and Pr160Gag-Pol processing intermediates that accumulate in primary and transformed cells treated with peptidic and nonpeptidic protease inhibitors
AU Speck, R. Renae; Flexner, Charles; Tian, Chun-Juan; Yu, Xiao-Fang
CS Departments of Pharmacology and Molecular Sciences, The Johns Hopkins University School of Medicine, Baltimore, MD, 21287-5554, USA
SO Antimicrobial Agents and Chemotherapy (2000), 44(5), 1397-1403
CODEN: AMACCQ; ISSN: 0066-4804
PB American Society for Microbiology
DT Journal
LA English
AB Human immunodeficiency virus type 1 (HIV-1) produces two polyproteins,

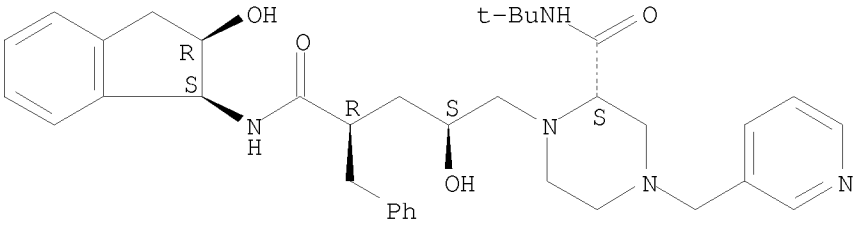
Pr55Gag and Pr160Gag-Pol, that are cleaved into mature functional subunits by the virally encoded protease. Drugs that inhibit this protease are an important part of anti-HIV therapy. We studied the ordered accumulation of Gag and Gag-Pol processing intermediates by variably blocking the protease with HIV-1 protease inhibitors (PIs). Variable protease inhibition caused accumulation of a complex pattern of processing intermediates, which was the same after incubating HIV-1-infected cells with increasing concns. of either one of the peptidomimetic inhibitors indinavir, saquinavir (SQV), ritonavir (RTV), nelfinavir, and SC-52151 or one of the nonpeptidomimetic inhibitors DMP450, DMP323, PNU-140135, and PNU-109112 for 3 days. The patterns of Gag and Gag-Pol processing intermediate accumulation were nearly identical when the following were compared: cell-vs. virion-associated proteins, HIV-1-infected transformed cell lines vs. primary human peripheral blood mononuclear cells (PBMCs) and HIV-1MN vs. HIV-1IIIB virus strains. RTV was a more potent inhibitor of p24 production in PBMCs than SQV by approx. 7-fold, whereas SQV was a more potent inhibitor in transformed cells than RTV by approx. 30-fold. Although the antiretroviral potency of HIV-1 PIs may change as a function of cell type, the polyprotein intermediates that accumulate with increasing drug concns. are the same. These results support sequential processing of Gag and Gag-Pol polyproteins by the HIV-1 protease and may have important implications for understanding common cross-resistance pathways.

IT 150378-17-9, Indinavir
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(comparison of HIV-1 Pr55Gag and Pr160Gag-Pol processing intermediates that accumulate in primary and transformed cells treated with peptidic and nonpeptidic protease inhibitors)

RN 150378-17-9 CAPLUS

CN D-erythro-Pentonamide, 2,3,5-trideoxy-N-[(1S,2R)-2,3-dihydro-2-hydroxy-1H-inden-1-yl]-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)- (CA INDEX NAME)

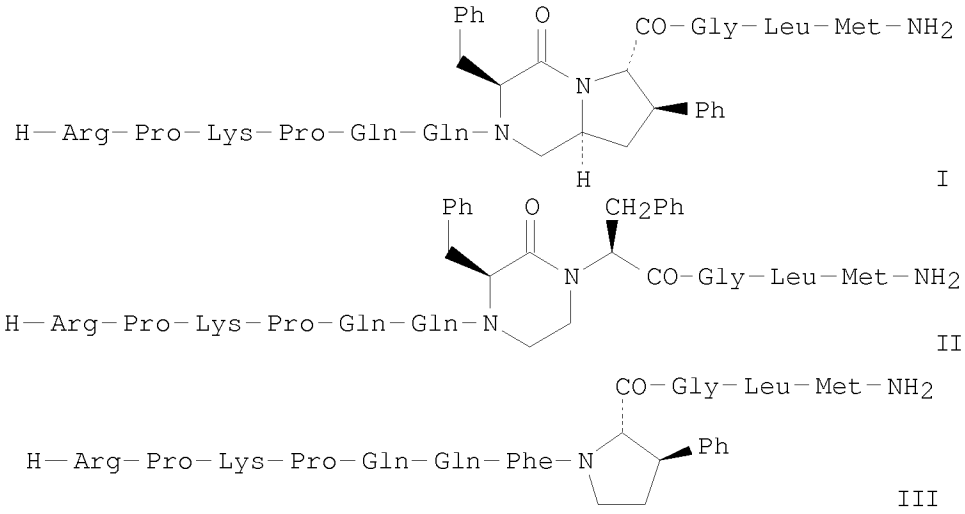
Absolute stereochemistry.



RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 13 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2000:188697 CAPLUS
DN 133:4959
TI Conformationally constrained substance P analogs: The total synthesis of a constrained peptidomimetic for the Phe7-Phe8 region
AU Tong, Yunsong; Fobian, Yvette M.; Wu, Meiye; Boyd, Norman D.; Moeller, Kevin D.
CS The Department of Chemistry, Washington University, St. Louis, MO, 63130, USA
SO Journal of Organic Chemistry (2000), 65(8), 2484-2493
CODEN: JOCEAH; ISSN: 0022-3263
PB American Chemical Society

DT Journal
LA English
GI



AB A bicyclic lactam I, peptidomimetic for the Phe7-Phe8 region of substance P, was synthesized. The synthesis used an anodic amide oxidation to selectively functionalize the C5-position of a 3-phenylproline derivative The resulting proline derivative was coupled to a Cbz-protected phenylalanine, and an intramol. reductive amination strategy used to convert the coupled material into a bicyclic piperazinone ring skeleton. The net result was a dipeptide building block that imbedded one of two proposed receptor bound conformations for the Phe7-Phe8 region of substance P into a bicyclic ring skeleton. The building block was then converted into a constrained substance P analog with the use of solid-phase peptide synthesis. A similar intramol. reductive amination strategy was used to synthesize a second substance P analog, piperazinone derivative II (only Phe7 constrained), and a third substance P analog, 3-phenylproline derivative III (only Phe8 constrained). All of the analogs were examined for their ability to displace substance P from its NK-1 receptor.

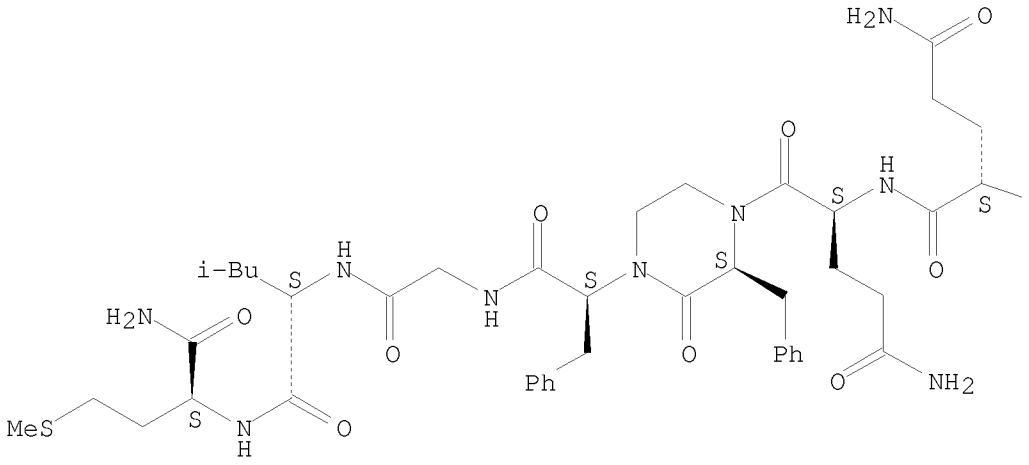
IT 212612-56-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of substance P analogs containing conformationally constrained Phe-Phe peptidomimetic)

RN 212612-56-1 CAPLUS

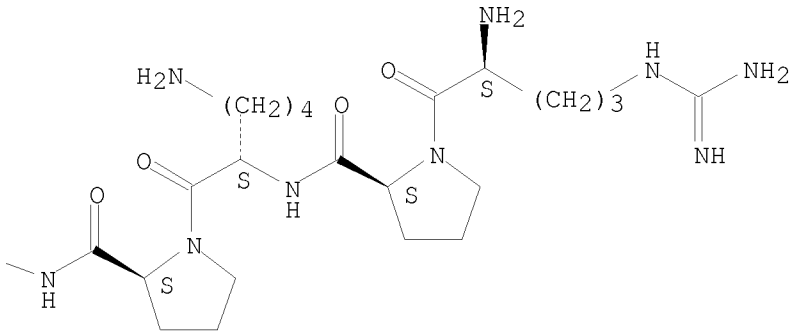
CN L-Methioninamide, L-arginyl-L-prolyl-L-lysyl-L-prolyl-L-glutaminyl-L-glutaminyl-(αS,3S)-2-oxo-α,3-bis(phenylmethyl)-1-piperazineacetylglycyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

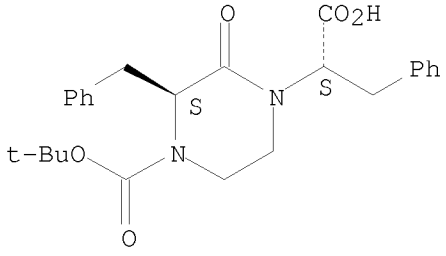


PAGE 1-B



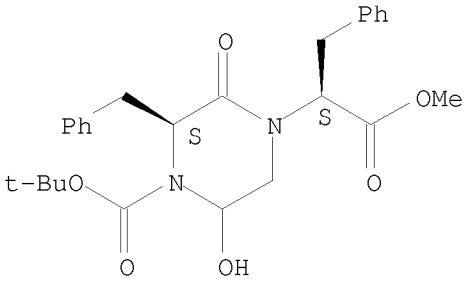
IT 193091-13-3P 270257-61-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of substance P analogs containing conformationally constrained Phe-Phe peptidomimetic)
RN 193091-13-3 CAPLUS
CN 1-Piperazineacetic acid, 4-[(1,1-dimethylethoxy)carbonyl]-2-oxo-α,3-bis(phenylmethyl)-, (αS,3S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



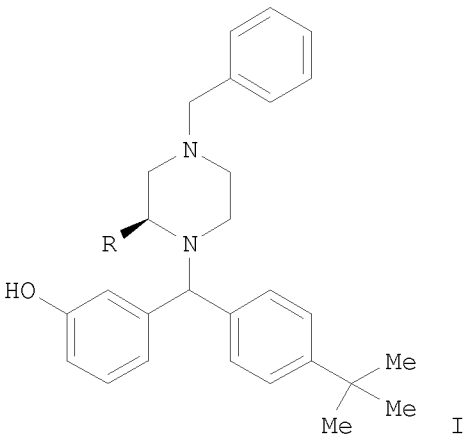
RN 270257-61-9 CAPLUS
CN 1-Piperazineacetic acid, 4-[(1,1-dimethylethoxy)carbonyl]-5-hydroxy-2-oxo-α,3-bis(phenylmethyl)-, methyl ester, (αS,3S)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 14 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1999:771172 CAPLUS
DN 132:102411
TI Exploring the Structure-Activity Relationships of [1-(4-tert-Butyl-3'-hydroxy)benzhydryl-4-benzylpiperazine] (SL-3111), A High-Affinity and Selective δ-Opioid Receptor Nonpeptide Agonist Ligand
AU Alfaro-Lopez, Josue; Okayama, Toru; Hosohata, Keiko; Davis, Peg; Porreca, Frank; Yamamura, Henry I.; Hruby, Victor J.
CS Departments of Chemistry and Pharmacology, The University of Arizona, Tucson, AZ, 85721, USA
SO Journal of Medicinal Chemistry (1999), 42(26), 5359-5368
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
GI



I

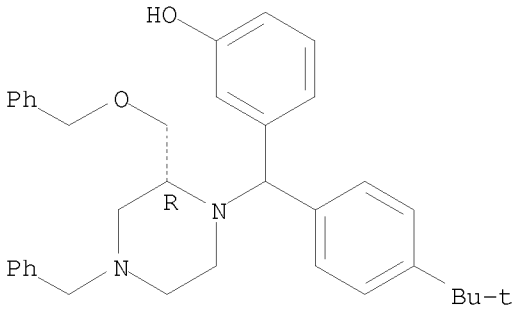
AB SL-3111 [1-(4-tert-butyl-3'-hydroxy)benzhydryl-4-benzylpiperazine] is a de novo designed, high-affinity and selective nonpeptide peptidomimetic agonist of the δ-opioid receptor. In a

previous report we had described the unique biol. characteristics of this ligand and also a need for further structural evaluation. To pursue this, we have introduced a completely different heterocyclic template, which based on mol. modeling studies, may present the required structural features to properly orient the pharmacophore groups. We also have made more subtle changes to the original piperazine scaffold. The biol. activities of these compds. revealed an important participation of the scaffold in the ligand-receptor interaction. To further explore functional diversity on the scaffold, we have maintained the original piperazine ring and introduced four different functionalities at position 2 of the heterocyclic ring (I; R = CH2-O-CH2-Ph; R = Me; R = CH2Ph; R = CH2OH). The biol. activities observed for these compds. showed a very interesting trend in terms of the steric effects of the groups introduced at this position. A decrease of almost 2000-fold in affinity and potency at the δ-receptor was observed for I (R = CH2Ph) compared with I (R = Me). This difference may be explained if we postulate that the bioactive conformation of these peptidomimetics is close to the minimal energy conformations calculated in our study. On the basis of these findings we have realized the importance of this position to further explore and simplify the structure of future generations of peptidomimetic ligands.

IT 255723-99-0P 255724-00-6P 255724-01-7P
255724-02-8P
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(preparation and structure-activity relationships of peptidomimetics based on SL-3111, a high-affinity and selective δ-opioid receptor nonpeptide agonist ligand)

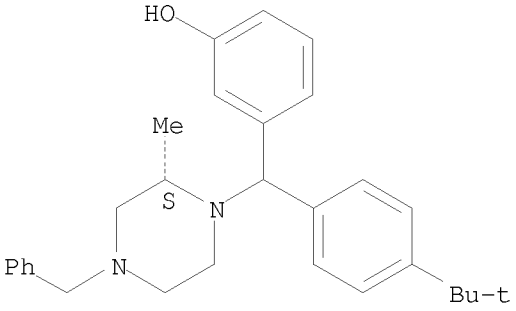
RN 255723-99-0 CAPLUS
CN Phenol, 3-[[4-(1,1-dimethylethyl)phenyl][(2R)-2-[(phenylmethoxy)methyl]-4-(phenylmethyl)-1-piperazinyl]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



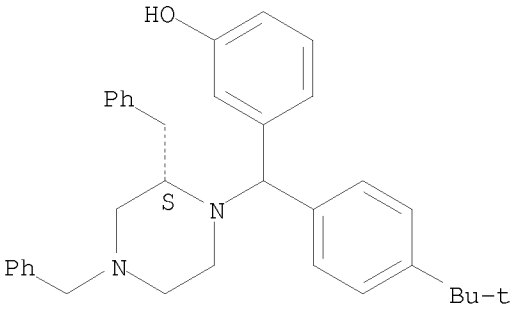
RN 255724-00-6 CAPLUS
CN Phenol, 3-[[4-(1,1-dimethylethyl)phenyl][(2S)-2-methyl-4-(phenylmethyl)-1-piperazinyl]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



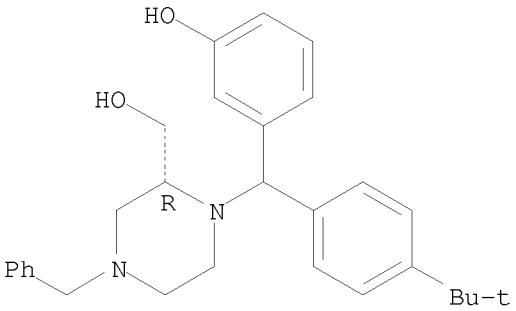
RN 255724-01-7 CAPLUS
CN Phenol, 3-[[(2S)-2,4-bis(phenylmethyl)-1-piperazinyl][4-(1,1-dimethylethyl)phenyl]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



RN 255724-02-8 CAPLUS
CN 2-Piperazinemethanol, 1-[[4-(1,1-dimethylethyl)phenyl](3-hydroxyphenyl)methyl]-4-(phenylmethyl)-, (2R)- (CA INDEX NAME)

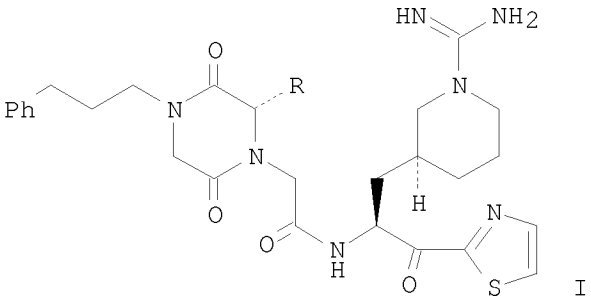
Absolute stereochemistry.



RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 15 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1999:614098 CAPLUS
DN 132:3352
TI The design of potent and selective inhibitors of thrombin utilizing a piperazinedione template. Part 1
AU Cody, Wayne L.; Cai, Cuiman; Doherty, Annette M.; Edmunds, Jeremy J.; He, John X.; Narasimhan, Lakshmi S.; Plummer, Janet S.; Rapundalo, Stephen T.;

Rubin, J. Ronald; Van Huis, Chad A.; St. Denis, Yves; Winocour, Peter D.; Siddiqui, M. Arshad
CS Parke-Davis Pharmaceutical Research, Division of Warner-Lambert Company, Ann Arbor, MI, 48105, USA
SO Bioorganic & Medicinal Chemistry Letters (1999), 9(17), 2497-2502
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
GI



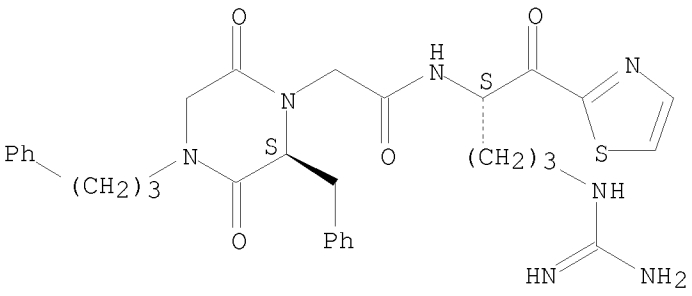
I

AB Utilizing X-ray crystallog. and mol. modeling, highly potent and selective peptidomimetic thrombin inhibitors have been designed containing a rigid piperazinedione template, I (R = CH2Ph, H, 3-pyridylmethyl, etc.). The synthesis and biol. activity of these compds. is described. The replacement of the benzyl group with aliphatic moieties led to compds. with reasonable selectivity for thrombin over trypsin. All of the compds. were relatively weak inhibitors. I [R = CH2(C6H11)] was the most potent among them.

IT 251308-18-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(preparation and thrombin inhibitory activity of thiazolyl (piperidinylmethyl) piperazinedione derivs.)

RN 251308-18-6 CAPLUS
CN 1-Piperazineacetamide, N-[(1S)-4-[(aminoiminomethyl)amino]-1-(2-thiazolylcarbonyl)butyl]-3,6-dioxo-2-(phenylmethyl)-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

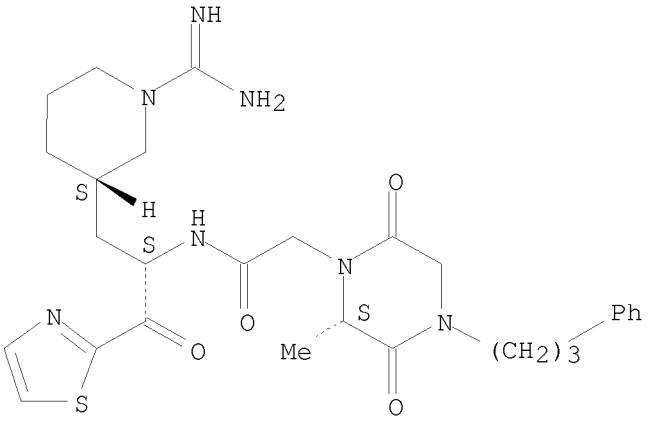


IT 204690-57-3P 204690-58-4P 204690-59-5P
204690-61-9P 204690-63-1P 204690-65-3P
204690-66-4P 204690-68-6P 204690-72-2P
204690-73-3P 251308-19-7P 251308-20-0P

251308-21-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and thrombin inhibitory activity of thiazolyl (piperidinylmethyl) piperazinedione derivs.)

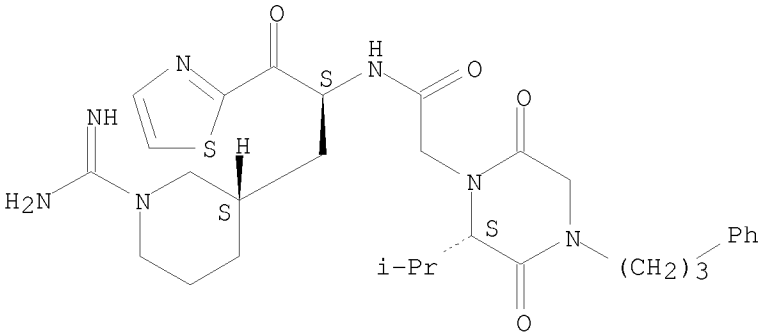
RN 204690-57-3 CAPLUS
CN 1-Piperazineacetamide, N-[(1S)-1-[[(3S)-1-(aminoiminomethyl)-3-piperidinyl]methyl]-2-oxo-2-(2-thiazolyl)ethyl]-2-methyl-3,6-dioxo-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



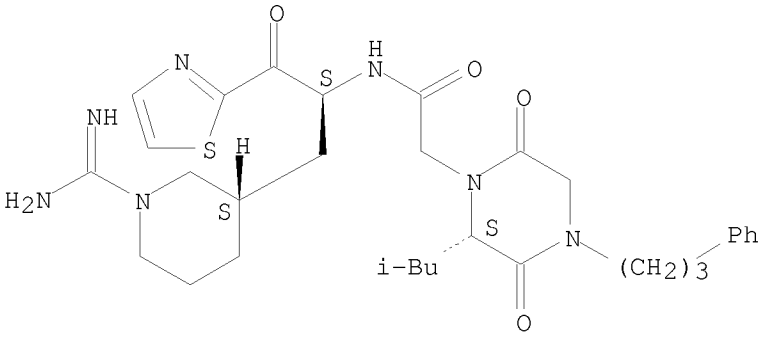
RN 204690-58-4 CAPLUS
CN 1-Piperazineacetamide, N-[(1S)-1-[[(3S)-1-(aminoiminomethyl)-3-piperidinyl]methyl]-2-oxo-2-(2-thiazolyl)ethyl]-2-(1-methylethyl)-3,6-dioxo-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



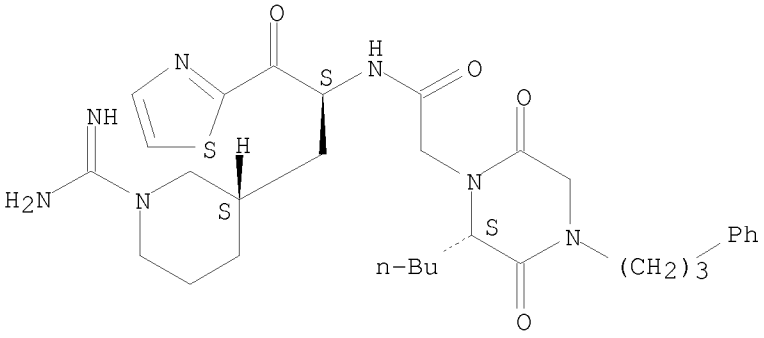
RN 204690-59-5 CAPLUS
CN 1-Piperazineacetamide, N-[(1S)-1-[[(3S)-1-(aminoiminomethyl)-3-piperidinyl]methyl]-2-oxo-2-(2-thiazolyl)ethyl]-2-(2-methylpropyl)-3,6-dioxo-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



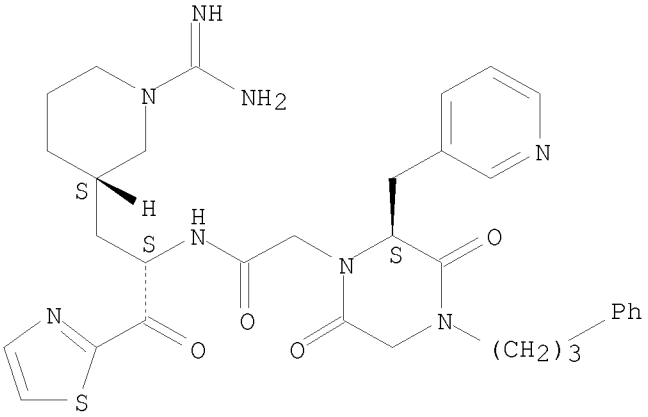
RN 204690-61-9 CAPLUS
CN 1-Piperazineacetamide, N-[(1S)-1-[[(3S)-1-(aminoiminomethyl)-3-piperidinyl]methyl]-2-oxo-2-(2-thiazolyl)ethyl]-2-butyl-3,6-dioxo-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 204690-63-1 CAPLUS
CN 1-Piperazineacetamide, N-[(1S)-1-[[(3S)-1-(aminoiminomethyl)-3-piperidinyl]methyl]-2-oxo-2-(2-thiazolyl)ethyl]-3,6-dioxo-4-(3-phenylpropyl)-2-(3-pyridinylmethyl)-, (2S)- (CA INDEX NAME)

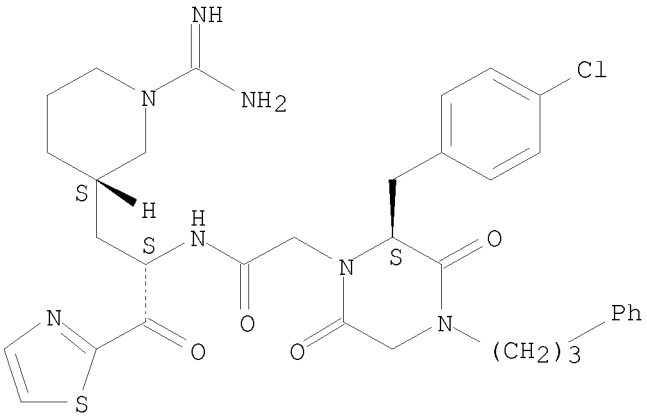
Absolute stereochemistry.



RN 204690-65-3 CAPLUS
CN 1-Piperazineacetamide, N-[(1S)-1-[[(3S)-1-(aminoiminomethyl)-3-

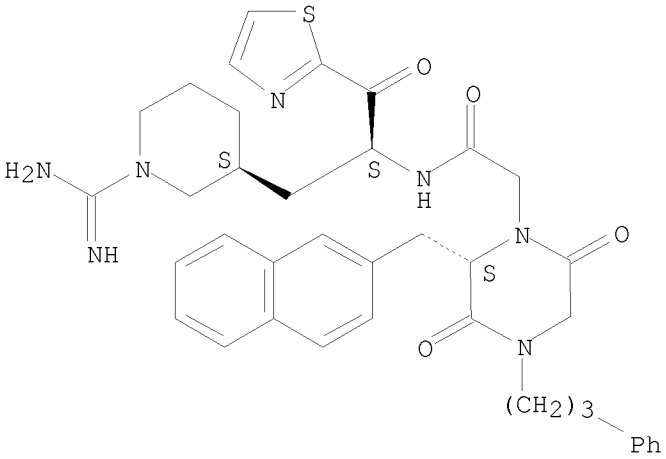
piperidinyl]methyl]-2-oxo-2-(2-thiazolyl)ethyl]-2-[(4-chlorophenyl)methyl]-3,6-dioxo-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



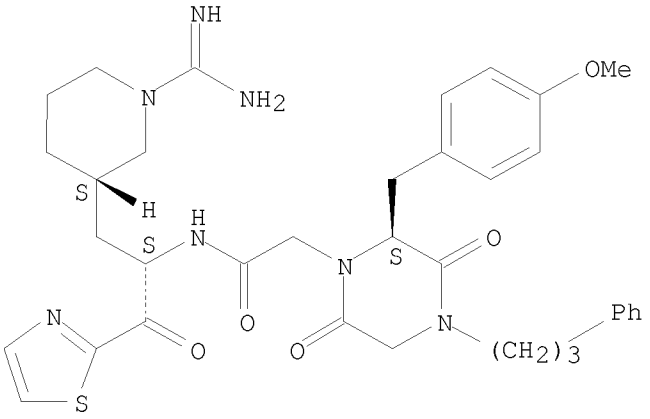
RN 204690-66-4 CAPLUS
CN 1-Piperazineacetamide, N-[(1S)-1-[[(3S)-1-(aminoiminomethyl)-3-piperidinyl]methyl]-2-oxo-2-(2-thiazolyl)ethyl]-2-(2-naphthalenylmethyl)-3,6-dioxo-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



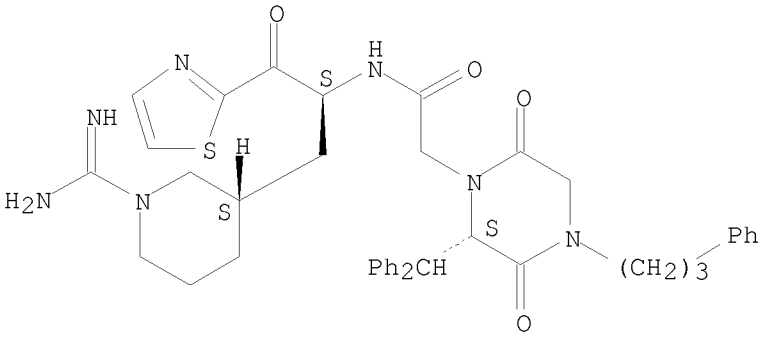
RN 204690-68-6 CAPLUS
CN 1-Piperazineacetamide, N-[(1S)-1-[[(3S)-1-(aminoiminomethyl)-3-piperidinyl]methyl]-2-oxo-2-(2-thiazolyl)ethyl]-2-[(4-methoxyphenyl)methyl]-3,6-dioxo-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



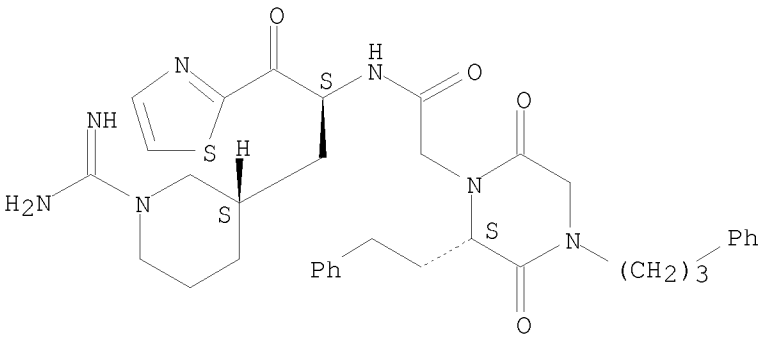
RN 204690-72-2 CAPLUS
CN 1-Piperazineacetamide, N-[(1S)-1-[[(3S)-1-(aminoiminomethyl)-3-piperidinyl]methyl]-2-oxo-2-(2-thiazolyl)ethyl]-2-(diphenylmethyl)-3,6-dioxo-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 204690-73-3 CAPLUS
CN 1-Piperazineacetamide, N-[(1S)-1-[[(3S)-1-(aminoiminomethyl)-3-piperidinyl]methyl]-2-oxo-2-(2-thiazolyl)ethyl]-3,6-dioxo-2-(2-phenylethyl)-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

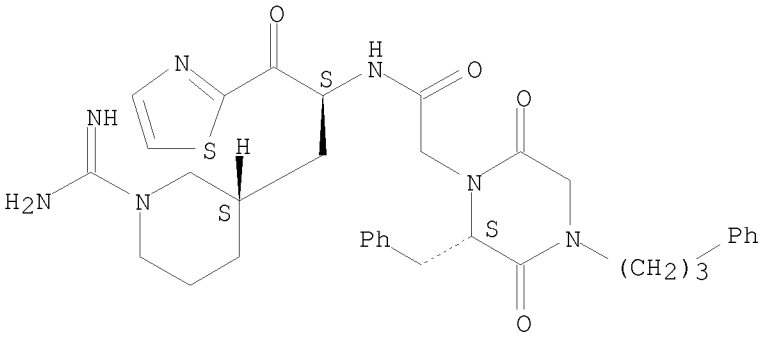
Absolute stereochemistry.



RN 251308-19-7 CAPLUS
CN 1-Piperazineacetamide, N-[(1S)-1-[[(3S)-1-(aminoiminomethyl)-3-

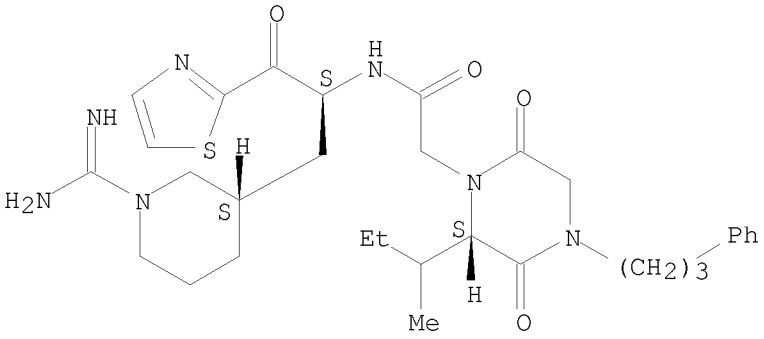
piperidinyl]methyl]-2-oxo-2-(2-thiazolyl)ethyl]-3,6-dioxo-2-(phenylmethyl)-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



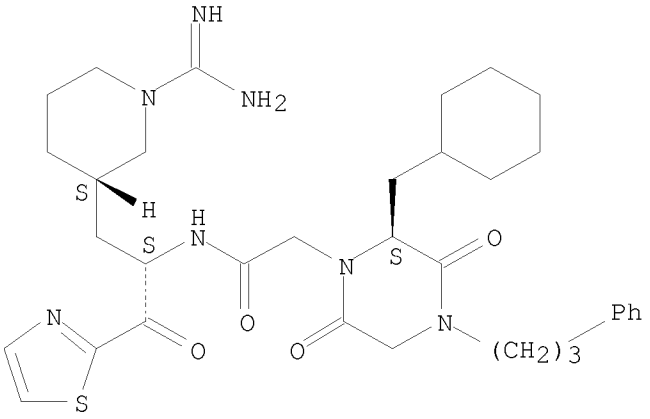
RN 251308-20-0 CAPLUS
CN 1-Piperazineacetamide, N-[(1S)-1-[[(3S)-1-(aminoiminomethyl)-3-piperidinyl]methyl]-2-oxo-2-(2-thiazolyl)ethyl]-2-(1-methylpropyl)-3,6-dioxo-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 251308-21-1 CAPLUS
CN 1-Piperazineacetamide, N-[(1S)-1-[[(3S)-1-(aminoiminomethyl)-3-piperidinyl]methyl]-2-oxo-2-(2-thiazolyl)ethyl]-2-(cyclohexylmethyl)-3,6-dioxo-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

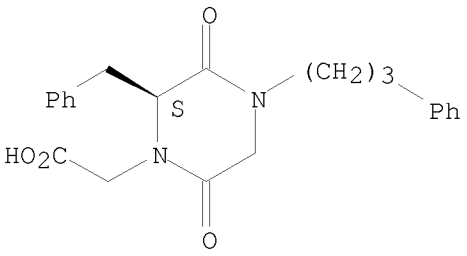


IT 204691-71-4P 251308-66-4P 251308-68-6P
251308-69-7P 251308-70-0P 251308-71-1P
251308-72-2P 251308-73-3P 251308-74-4P
251308-75-5P 251308-76-6P 251308-77-7P
251308-78-8P 251308-79-9P 251308-81-3P
251308-82-4P 251308-83-5P 251308-84-6P
251308-85-7P 251308-86-8P 251308-87-9P
251308-88-0P 251308-89-1P 251308-90-4P
251308-91-5P 251308-92-6P 251308-94-8P
251308-96-0P 251308-97-1P 251308-98-2P
251308-99-3P 251309-00-9P 251309-01-0P
251309-02-1P 251309-03-2P 251309-04-3P
251309-05-4P 251309-06-5P 251309-08-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and thrombin inhibitory activity of thiazolyl (piperidinylmethyl) piperazinedione derivs.)

RN 204691-71-4 CAPLUS

CN 1-Piperazineacetic acid, 3,6-dioxo-2-(phenylmethyl)-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

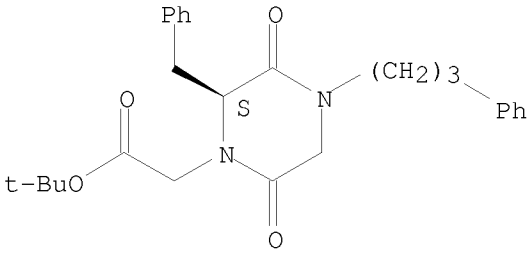
Absolute stereochemistry.



RN 251308-66-4 CAPLUS

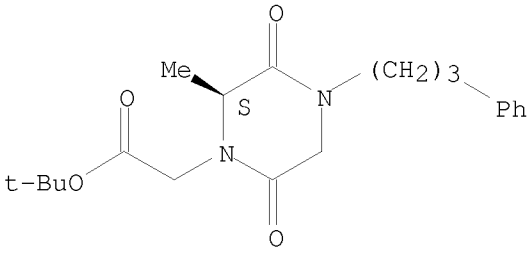
CN 1-Piperazineacetic acid, 3,6-dioxo-2-(phenylmethyl)-4-(3-phenylpropyl)-, 1,1-dimethylethyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



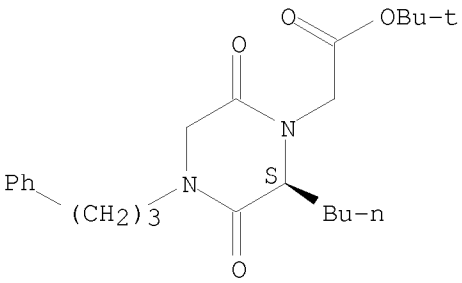
RN 251308-68-6 CAPLUS
CN 1-Piperazineacetic acid, 2-methyl-3,6-dioxo-4-(3-phenylpropyl)-, 1,1-dimethylethyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



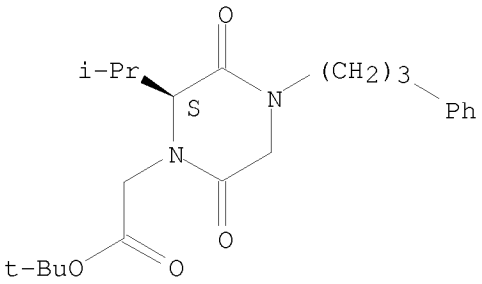
RN 251308-69-7 CAPLUS
CN 1-Piperazineacetic acid, 2-butyl-3,6-dioxo-4-(3-phenylpropyl)-, 1,1-dimethylethyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



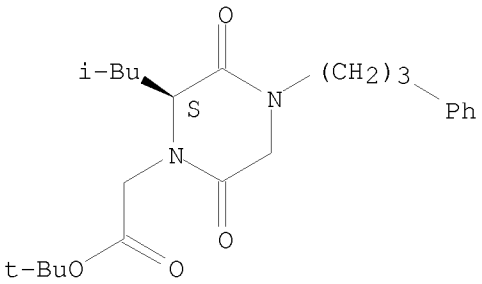
RN 251308-70-0 CAPLUS
CN 1-Piperazineacetic acid, 2-(1-methylethyl)-3,6-dioxo-4-(3-phenylpropyl)-, 1,1-dimethylethyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



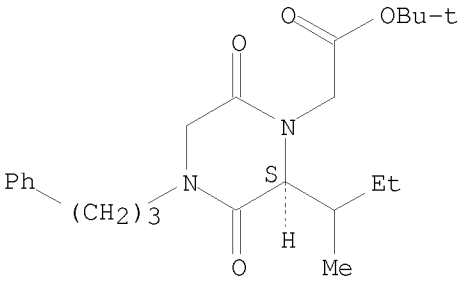
RN 251308-71-1 CAPLUS
CN 1-Piperazineacetic acid, 2-(2-methylpropyl)-3,6-dioxo-4-(3-phenylpropyl)-, 1,1-dimethylethyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



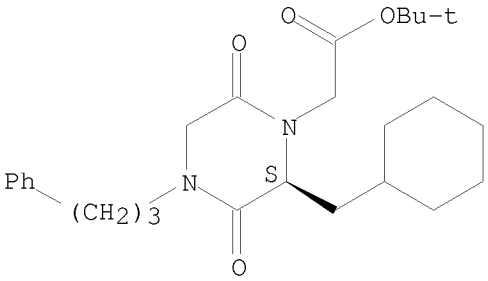
RN 251308-72-2 CAPLUS
CN 1-Piperazineacetic acid, 2-(1-methylpropyl)-3,6-dioxo-4-(3-phenylpropyl)-, 1,1-dimethylethyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



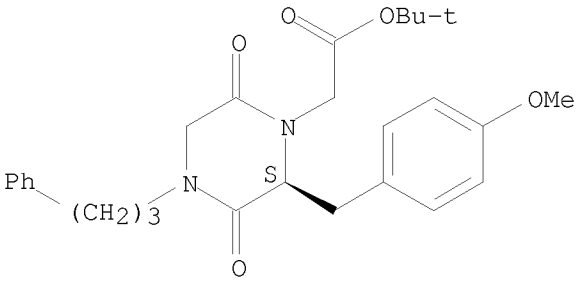
RN 251308-73-3 CAPLUS
CN 1-Piperazineacetic acid, 2-(cyclohexylmethyl)-3,6-dioxo-4-(3-phenylpropyl)-, 1,1-dimethylethyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



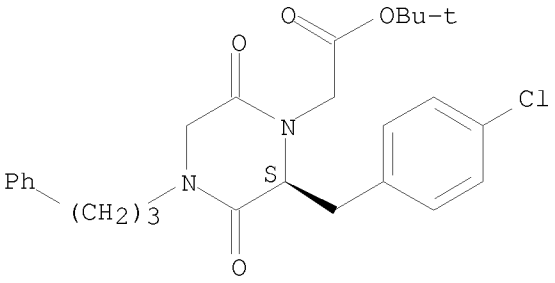
RN 251308-74-4 CAPLUS
CN 1-Piperazineacetic acid, 2-[(4-methoxyphenyl)methyl]-3,6-dioxo-4-(3-phenylpropyl)-, 1,1-dimethylethyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



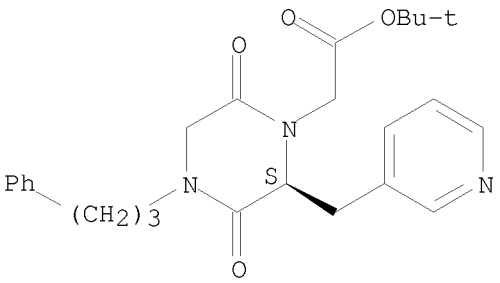
RN 251308-75-5 CAPLUS
CN 1-Piperazineacetic acid, 2-[(4-chlorophenyl)methyl]-3,6-dioxo-4-(3-phenylpropyl)-, 1,1-dimethylethyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



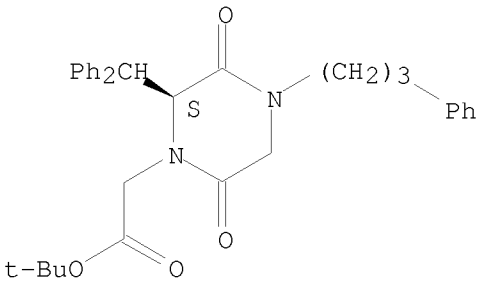
RN 251308-76-6 CAPLUS
CN 1-Piperazineacetic acid, 3,6-dioxo-4-(3-phenylpropyl)-2-(3-pyridinylmethyl)-, 1,1-dimethylethyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



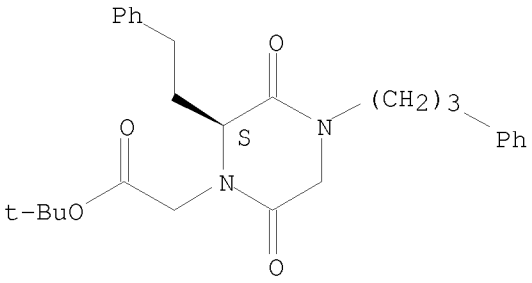
RN 251308-77-7 CAPLUS
CN 1-Piperazineacetic acid, 2-(diphenylmethyl)-3,6-dioxo-4-(3-phenylpropyl)-, 1,1-dimethylethyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



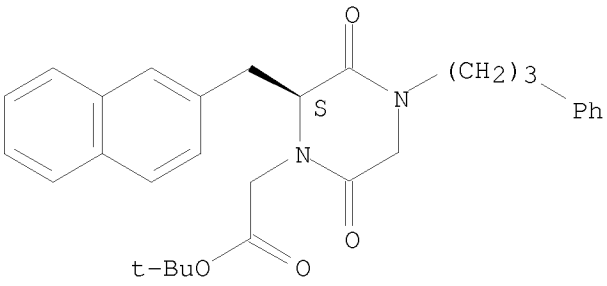
RN 251308-78-8 CAPLUS
CN 1-Piperazineacetic acid, 3,6-dioxo-2-(2-phenylethyl)-4-(3-phenylpropyl)-, 1,1-dimethylethyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



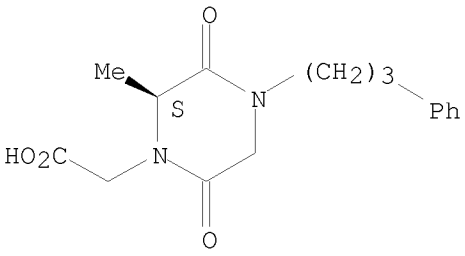
RN 251308-79-9 CAPLUS
CN 1-Piperazineacetic acid, 2-(2-naphthalenylmethyl)-3,6-dioxo-4-(3-phenylpropyl)-, 1,1-dimethylethyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



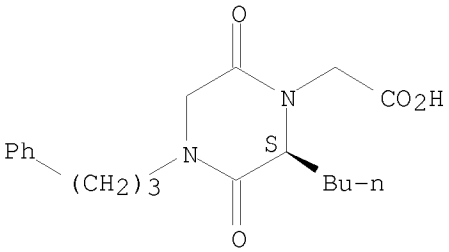
RN 251308-81-3 CAPLUS
CN 1-Piperazineacetic acid, 2-methyl-3,6-dioxo-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



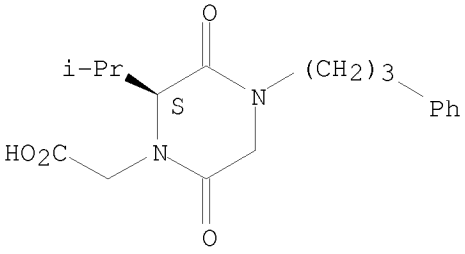
RN 251308-82-4 CAPLUS
CN 1-Piperazineacetic acid, 2-butyl-3,6-dioxo-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



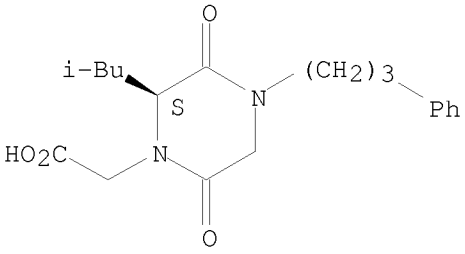
RN 251308-83-5 CAPLUS
CN 1-Piperazineacetic acid, 2-(1-methylethyl)-3,6-dioxo-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



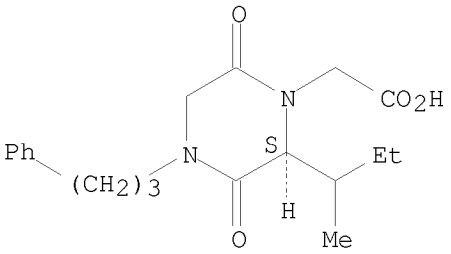
RN 251308-84-6 CAPLUS
CN 1-Piperazineacetic acid, 2-(2-methylpropyl)-3,6-dioxo-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



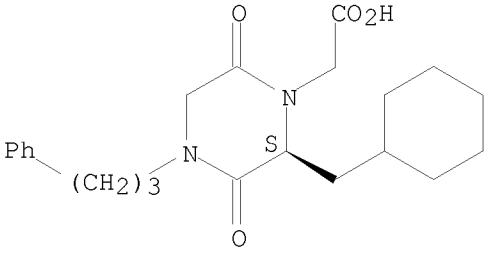
RN 251308-85-7 CAPLUS
CN 1-Piperazineacetic acid, 2-(1-methylpropyl)-3,6-dioxo-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



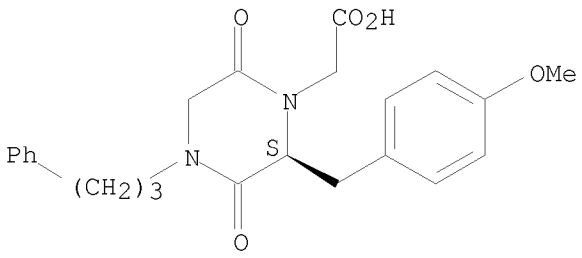
RN 251308-86-8 CAPLUS
CN 1-Piperazineacetic acid, 2-(cyclohexylmethyl)-3,6-dioxo-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



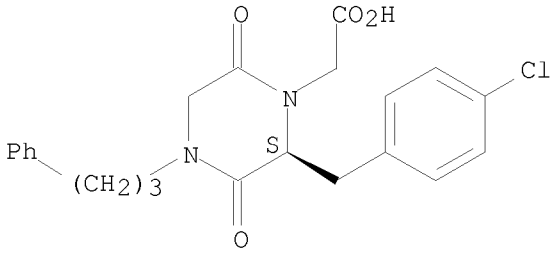
RN 251308-87-9 CAPLUS
CN 1-Piperazineacetic acid, 2-[(4-methoxyphenyl)methyl]-3,6-dioxo-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



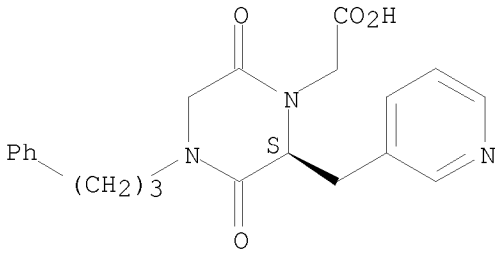
RN 251308-88-0 CAPLUS
CN 1-Piperazineacetic acid, 2-[(4-chlorophenyl)methyl]-3,6-dioxo-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



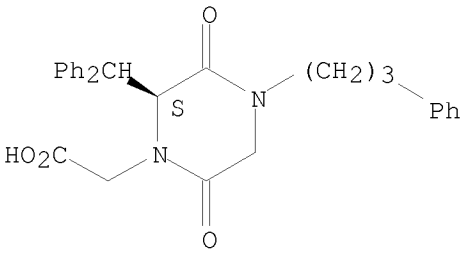
RN 251308-89-1 CAPLUS
CN 1-Piperazineacetic acid, 3,6-dioxo-4-(3-phenylpropyl)-2-(3-pyridinylmethyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



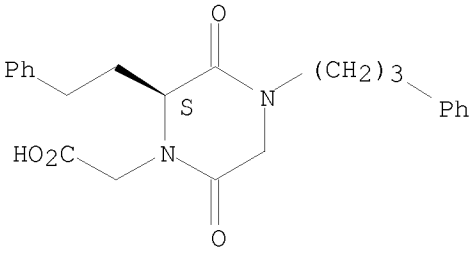
RN 251308-90-4 CAPLUS
CN 1-Piperazineacetic acid, 2-(diphenylmethyl)-3,6-dioxo-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



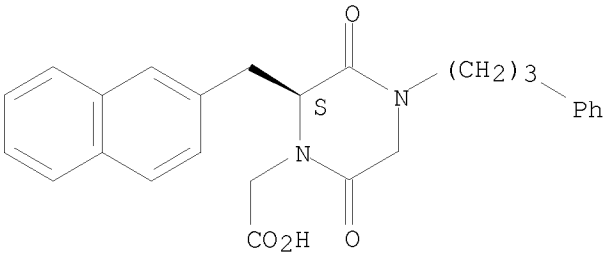
RN 251308-91-5 CAPLUS
CN 1-Piperazineacetic acid, 3,6-dioxo-2-(2-phenylethyl)-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 251308-92-6 CAPLUS
CN 1-Piperazineacetic acid, 2-(2-naphthalenylmethyl)-3,6-dioxo-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 251308-94-8 CAPLUS
CN 1-Piperazineacetamide, N-[(1S)-1-[[(3S)-1-[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]-3-piperidinyl]methyl]-2-oxo-2-(2-thiazolyl)ethyl]-3,6-dioxo-2-(phenylmethyl)-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

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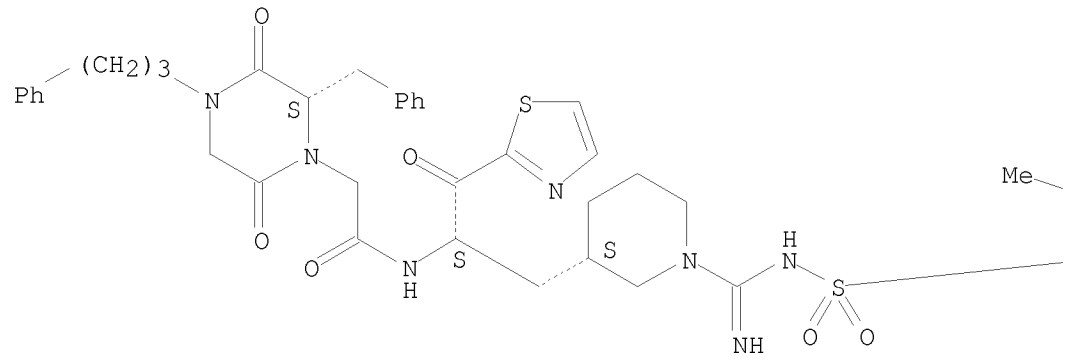

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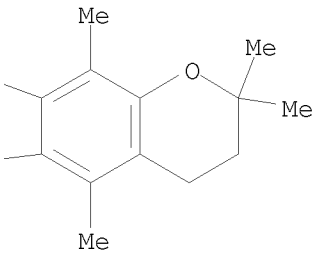

RN 251308-96-0 CAPLUS
CN 1-Piperazineacetamide, N-[(1S)-1-[[(3S)-1-[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]-3-piperidinyl]methyl]-2-oxo-2-(2-thiazolyl)ethyl]-2-methyl-3,6-dioxo-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

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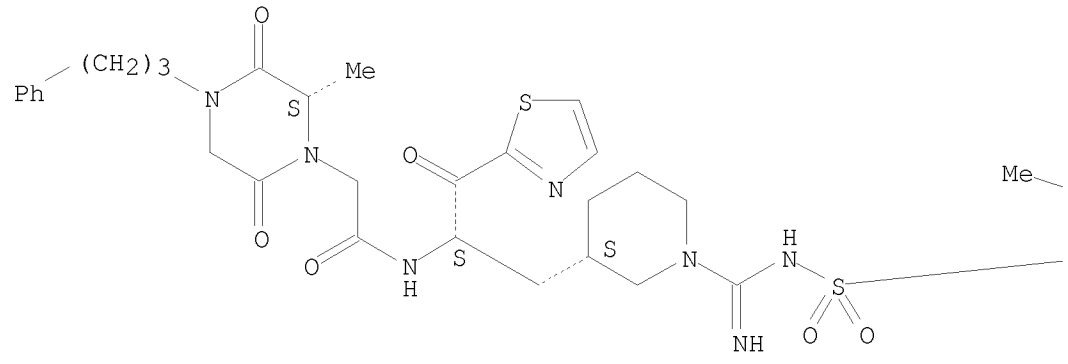

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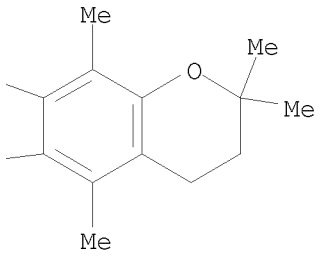

RN 251308-97-1 CAPLUS
CN 1-Piperazineacetamide, 2-butyl-N-[(1S)-1-[[(3S)-1-[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]-3-piperidinyl]methyl]-2-oxo-2-(2-thiazolyl)ethyl]-3,6-dioxo-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

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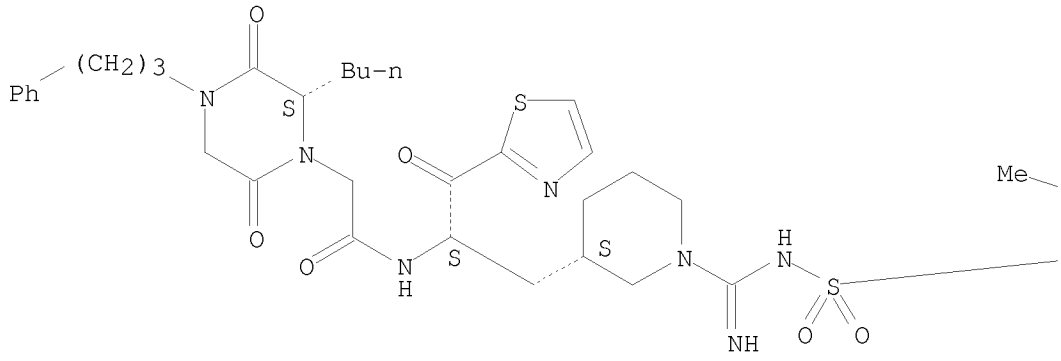

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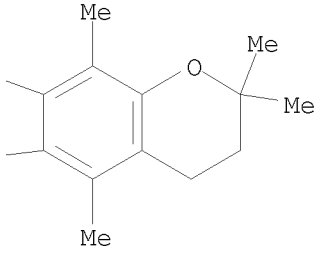

RN 251308-98-2 CAPLUS
CN 1-Piperazineacetamide, N-[(1S)-1-[[(3S)-1-[[[(3,4-dihydro-2,2,5,7,8-

pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]-3-piperidinyl]methyl]-2-oxo-2-(2-thiazolyl)ethyl]-2-(1-methylethyl)-3,6-dioxo-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

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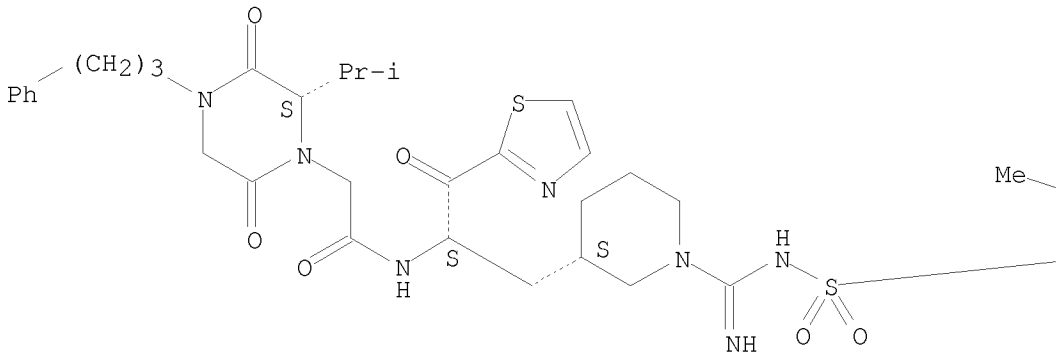

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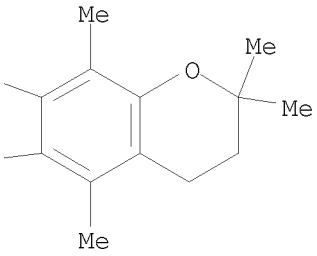

RN 251308-99-3 CAPLUS

CN 1-Piperazineacetamide, N-[(1S)-1-[[(3S)-1-[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]-3-piperidinyl]methyl]-2-oxo-2-(2-thiazolyl)ethyl]-2-(2-methylpropyl)-3,6-dioxo-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

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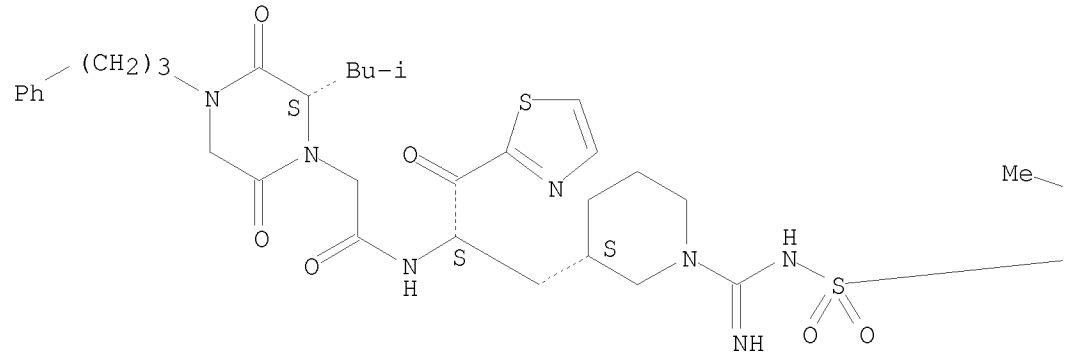

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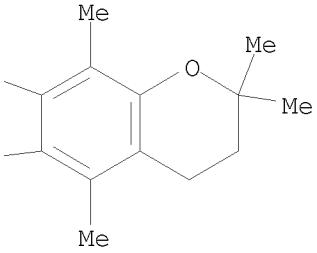

RN 251309-00-9 CAPLUS
CN 1-Piperazineacetamide, N-[(1S)-1-[[(3S)-1-[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]-3-piperidinyl]methyl]-2-oxo-2-(2-thiazolyl)ethyl]-2-(1-methylpropyl)-3,6-dioxo-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

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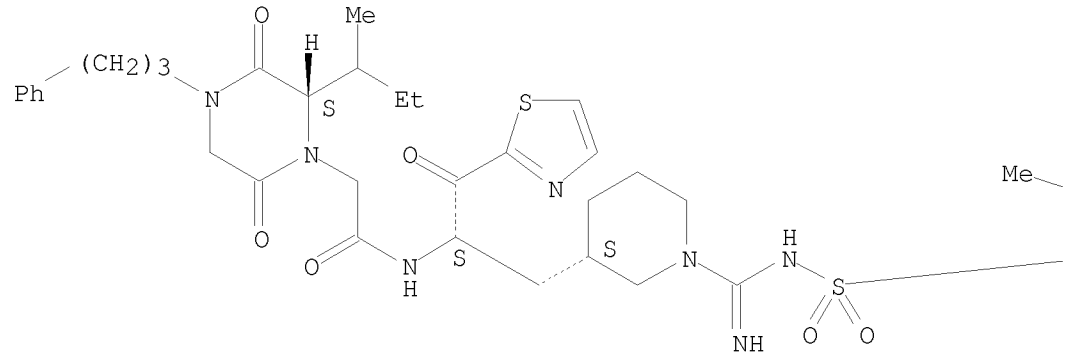

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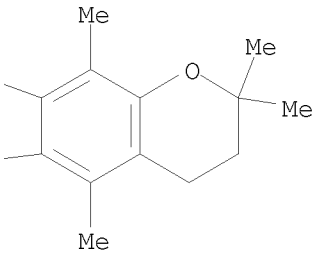
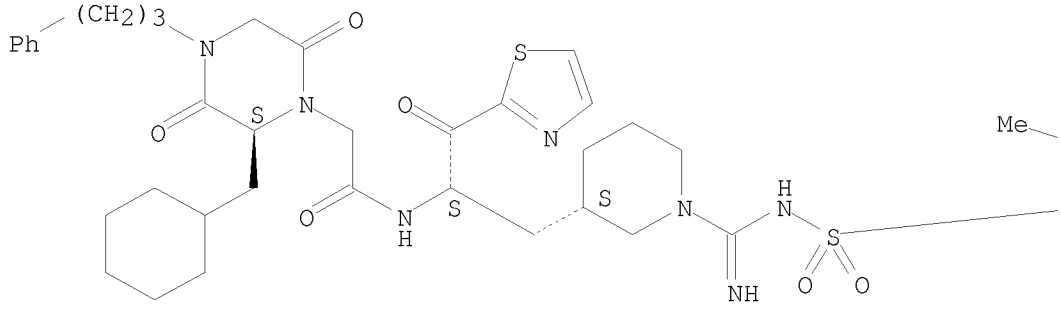


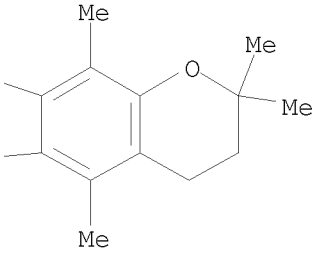
RN 251309-01-0 CAPLUS
CN 1-Piperazineacetamide, 2-(cyclohexylmethyl)-N-[(1S)-1-[[(3S)-1-[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]-3-piperidinyl]methyl]-2-oxo-2-(2-thiazolyl)ethyl]-3,6-dioxo-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



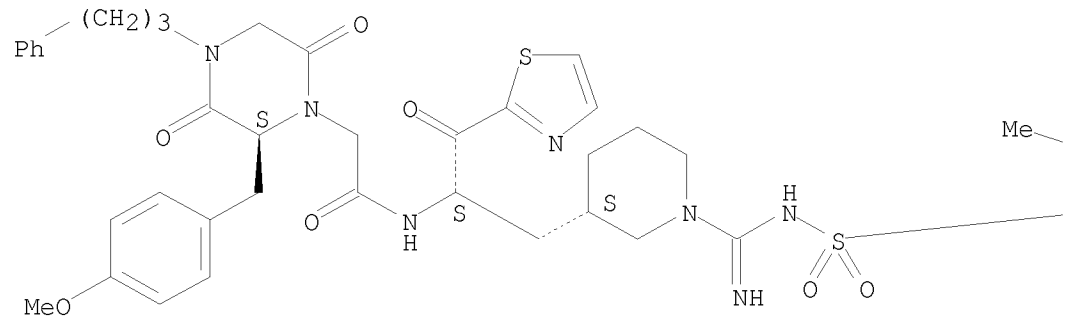
PAGE 1-B



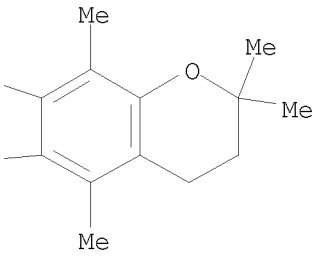
RN 251309-02-1 CAPLUS
CN 1-Piperazineacetamide, N-[(1S)-1-[[(3S)-1-[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]-3-piperidinyl]methyl]-2-oxo-2-(2-thiazolyl)ethyl]-2-[(4-methoxyphenyl)methyl]-3,6-dioxo-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



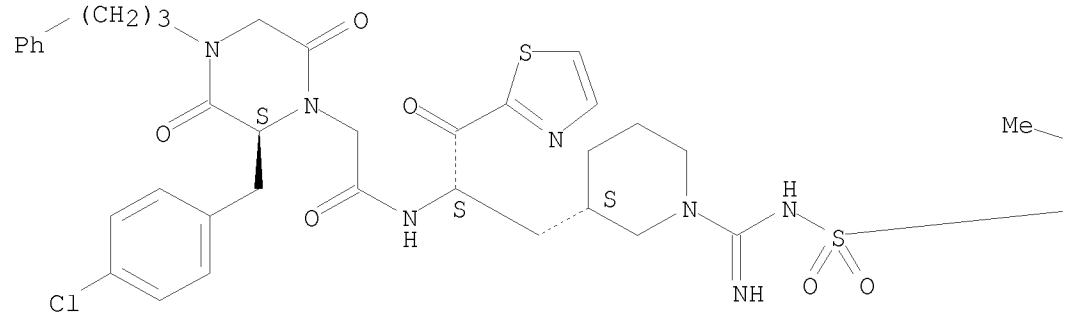
PAGE 1-B



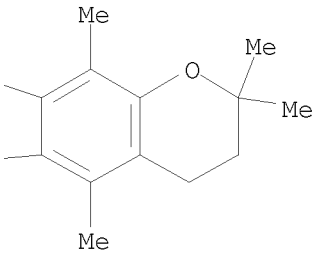
RN 251309-03-2 CAPLUS
CN 1-Piperazineacetamide, 2-[(4-chlorophenyl)methyl]-N-[(1S)-1-[[(3S)-1-[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]-3-piperidinyl]methyl]-2-oxo-2-(2-thiazolyl)ethyl]-3,6-dioxo-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



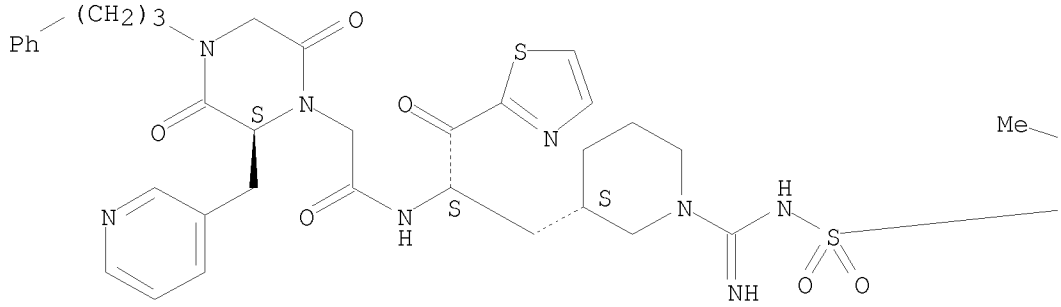
PAGE 1-B



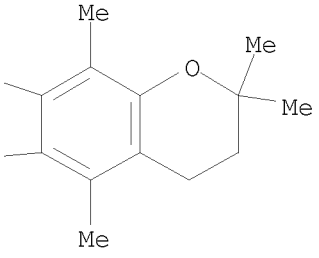
RN 251309-04-3 CAPLUS
CN 1-Piperazineacetamide, N-[(1S)-1-[[(3S)-1-[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]-3-piperidinyl]methyl]-2-oxo-2-(2-thiazolyl)ethyl]-3,6-dioxo-4-(3-phenylpropyl)-2-(3-pyridinylmethyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



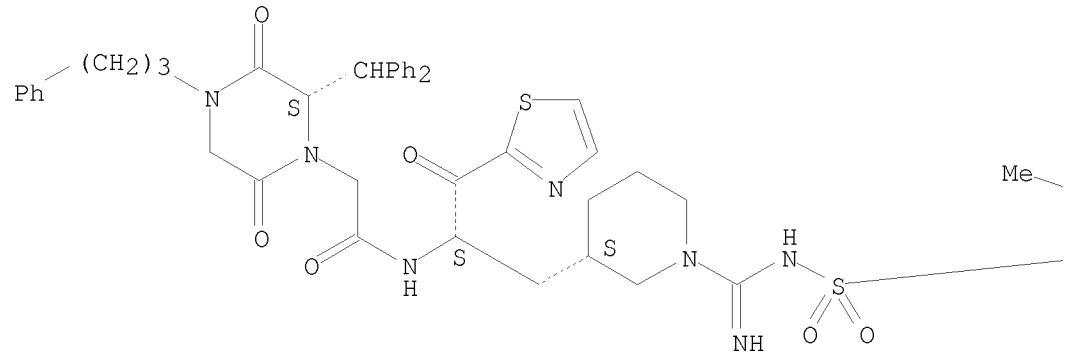
PAGE 1-B



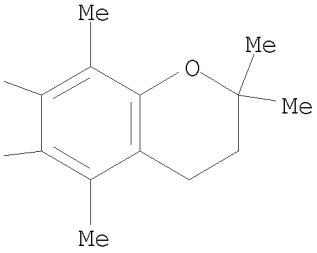
RN 251309-05-4 CAPLUS
CN 1-Piperazineacetamide, N-[(1S)-1-[[(3S)-1-[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]-3-piperidinyl]methyl]-2-oxo-2-(2-thiazolyl)ethyl]-2-(diphenylmethyl)-3,6-dioxo-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



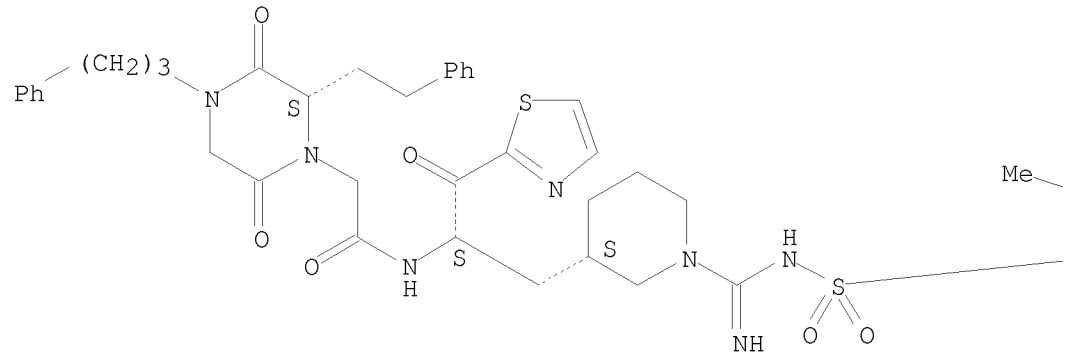
PAGE 1-B



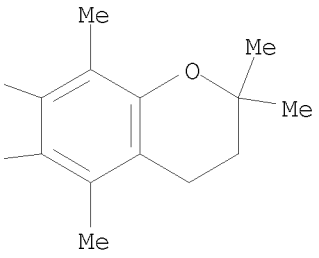
RN 251309-06-5 CAPLUS
CN 1-Piperazineacetamide, N-[(1S)-1-[[(3S)-1-[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]-3-piperidinyl]methyl]-2-oxo-2-(2-thiazolyl)ethyl]-3,6-dioxo-2-(2-phenylethyl)-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



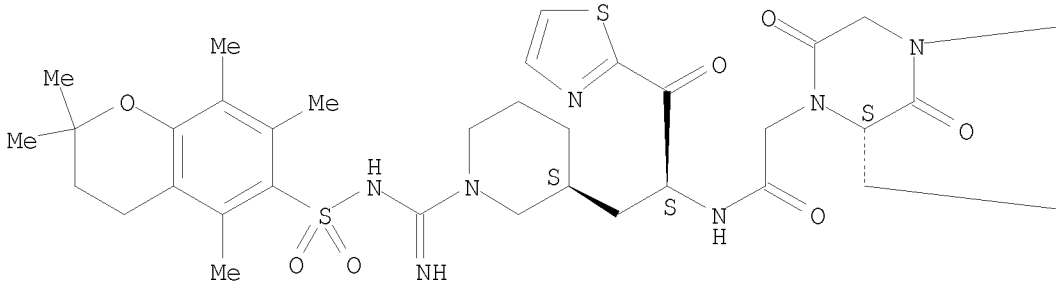
PAGE 1-B



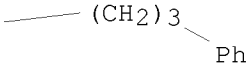
RN 251309-08-7 CAPLUS
CN 1-Piperazineacetamide, N-[(1S)-1-[[(3S)-1-[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]-3-piperidinyl]methyl]-2-oxo-2-(2-thiazolyl)ethyl]-2-(2-naphthalenylmethyl)-3,6-dioxo-4-(3-phenylpropyl)-, (2S)- (CA INDEX NAME)

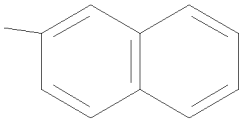
Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

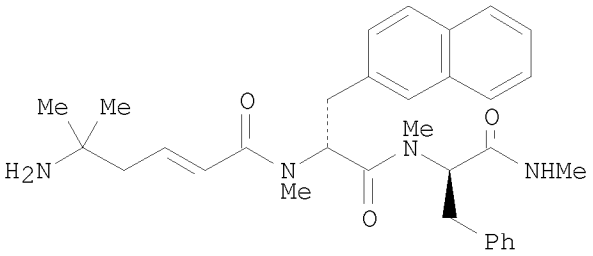




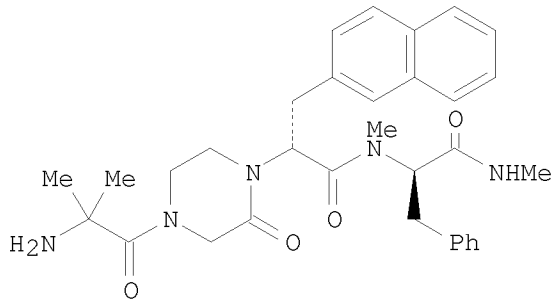
RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 16 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1999:292485 CAPLUS
DN 131:32160
TI Synthesis of piperazinones and their application in constrained mimetics of the growth hormone secretagogue NN-703

AU Hansen, Thomas K.; Schlienger, Nathalie; Hansen, Birgit S.; Andersen, Peter H.; Bryce, Martin R.
CS Medicinal Chemistry Research, Novo Nordisk A/S, Malov, 2760, Den.
SO Tetrahedron Letters (1999), 40(18), 3651-3654
CODEN: TELEAY; ISSN: 0040-4039
PB Elsevier Science Ltd.
DT Journal
LA English
GI



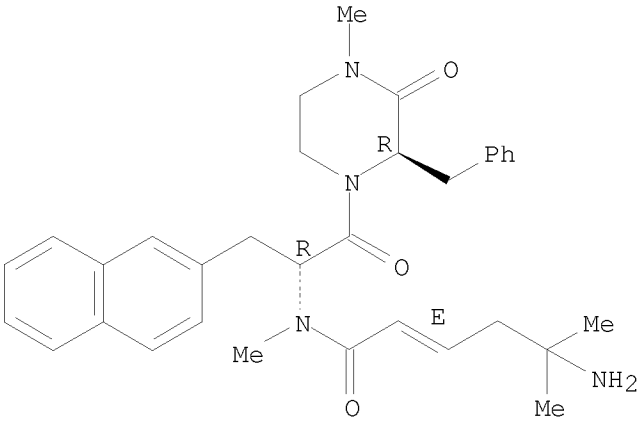
I



II

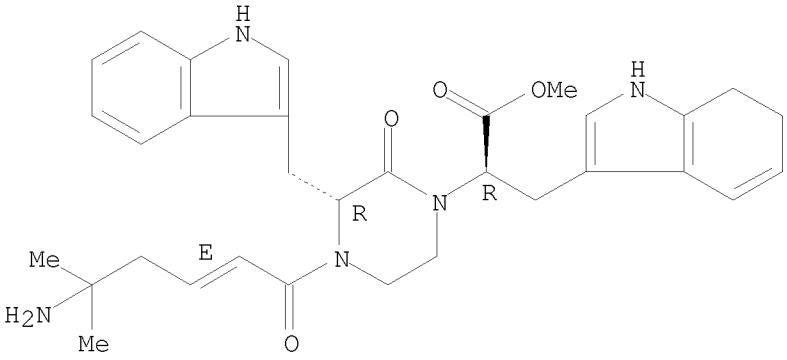
AB The chemical of 2-piperazinones and the use of this building block to restrict the conformational freedom of the growth hormone secretagogue NN-703 (I; currently in clin. development) is reported here. The authors used classical methods for 2-piperazinone synthesis as well as some novel approaches such as a Boronic Mannich reaction. The authors, also, studied the ability of these constrained, piperazinone-based target compds. to release growth hormone in vitro. For example, piperazinone II was synthesized and was able to release growth hormone in-vitro at a concentration of 600 nM, compared to 18 nM concentration of I.
IT 198973-69-2P 226890-56-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); BIOL (Biological study); PREP (Preparation)
(synthesis and biol. activity of piperazinone-containing peptidomimetics as constrained analogs of the growth hormone secretagogue NN-703)
RN 198973-69-2 CAPLUS
CN 2-Hexenamide, 5-amino-N,5-dimethyl-N-[(1R)-2-[(2R)-4-methyl-3-oxo-2-(phenylmethyl)-1-piperazinyl]-1-(2-naphthalenylmethyl)-2-oxoethyl]-, (2E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



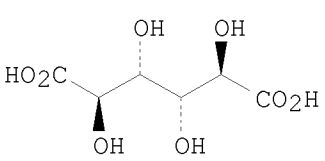
RN 226890-56-8 CAPLUS
CN 1H-Indole-3-propanoic acid, α-[(3R)-4-[(2E)-5-amino-5-methyl-1-oxo-2-hexenyl]-3-(1H-indol-3-ylmethyl)-2-oxo-1-piperazinyl]-6,7-dihydro-, methyl ester, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

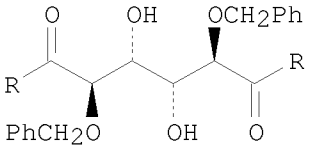


RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

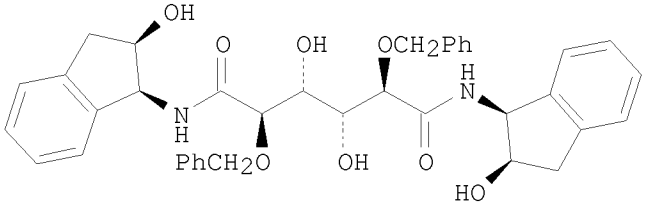
L8 ANSWER 17 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1998:548966 CAPLUS
DN 129:276304
TI Design and Synthesis of New Potent C2-Symmetric HIV-1 Protease Inhibitors. Use of L-Mannaric Acid as a Peptidomimetic Scaffold
AU Alterman, Mathias; Bjoersne, Magnus; Muehlman, Anna; Classon, Bjoern; Kvarnstroem, Ingemar; Danielson, Helena; Markgren, Per-Olof; Nillroth, Ulrika; Unge, Torsten; Hallberg, Anders; Samuelsson, Bertil
CS Department of Chemistry, Linkoeping University, Linkoeping, S-581 83, Swed.
SO Journal of Medicinal Chemistry (1998), 41(20), 3782-3792
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
GI



I



II



III

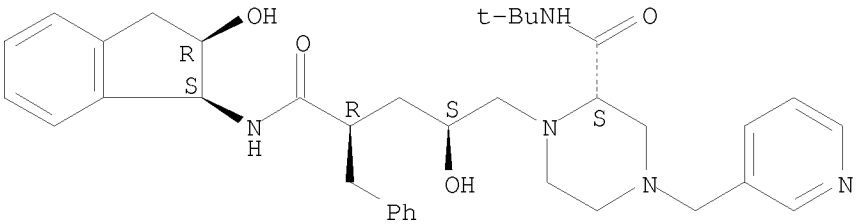
AB A study on the use of derivatized carbohydrates as C2-sym. HIV-1 protease inhibitors has been undertaken. L-Mannaric acid (I) was bis-O-benzylated at C-2 and C-5 and subsequently coupled with amino acids and amines to give C2-sym. products based on C-terminal duplication. Potent HIV protease inhibitors, II (R = Val-NHMe) (Ki = 0.4 nM) and III (Ki = 0.2 nM), have been discovered, and two synthetic methodologies have been developed, one whereby these inhibitors can be prepared in just three chemical steps from com. available materials. A remarkable increase in potency going from II (R = Val-OMe) (IC50 = 5000 nM) to II (R = Val-NHMe) (IC50 = 15 nM) was observed, resulting in the net addition of one hydrogen bond interaction between each of the two NH groups and the HIV protease backbone (Gly 48/148). The x-ray crystal structures of III and of II (R = Ile-NHMe) have been determined, revealing the binding mode of these inhibitors which will aid further design.

IT 150378-17-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(use of mannaric acid as peptidomimetic scaffold in design and synthesis of new potent C2-sym. HIV-1 protease inhibitors)

RN 150378-17-9 CAPLUS

CN D-erythro-Pentonamide, 2,3,5-trideoxy-N-[(1S,2R)-2,3-dihydro-2-hydroxy-1H-inden-1-yl]-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 18 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1998:497694 CAPLUS
DN 129:227870
TI Protein prenyl transferase activities of Plasmodium falciparum

AU Chakrabarti, Debopam; Azam, Tania; DelVecchio, Cherie; Qiu, Libo; Park, Yong-il; Allen, Charles M.

CS Microbiology and Center for Diagnostics and Drug Development, Department of Molecular Biology, University of Central Florida, Orlando, FL, 322816-2360, USA

SO Molecular and Biochemical Parasitology (1998), 94(2), 175-184
CODEN: MBIPDP; ISSN: 0166-6851
PB Elsevier Science B.V.
DT Journal
LA English

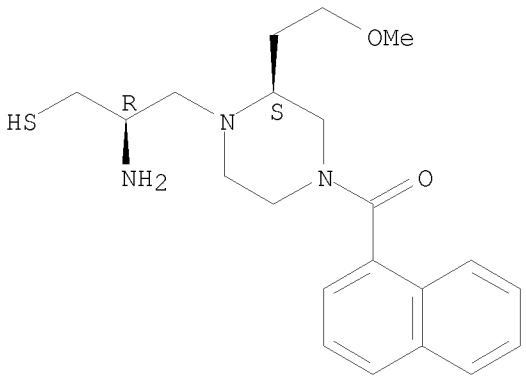
AB Prenylated proteins have been shown to function in important cellular regulatory processes, including signal transduction. The enzymes involved in protein prenylation, farnesyl transferase and geranylgeranyl transferase, have been recent targets for development of cancer chemotherapeutics. We have initiated a systematic study of protein prenyl transferases of the malaria parasite, Plasmodium falciparum, to determine whether these enzymes can be developed as targets for antimalarial chemotherapy. We report here the identification of protein farnesyl transferase and protein geranylgeranyl transferase-I in the malaria parasite, P. falciparum. The farnesyl transferase has been partially purified from the cytosolic fraction through ammonium sulfate precipitation and Mono-Q chromatog. Farnesyl and geranylgeranyl transferase-I activities are present at all stages of P. falciparum intraerythrocytic development with maximum specific activity in the ring stage. Geranylgeranyl transferase-I specific activity is two times that of farnesyl transferase in the ring stage. Peptidomimetics and prenyl analogs of protein farnesyl transferase substrates were tested as in vitro inhibitors of partially purified P. falciparum prenyl transferase and of malaria parasite growth. The peptidomimetics were significantly more potent inhibitors than lipid substrate analogs of both the activity of Mono-Q purified enzyme and parasite growth in intraerythrocytic cultures. Exposure of the parasite to the peptidomimetic L-745,631 also showed significant inhibition of morphol. development beyond the trophozoite stage. These studies suggest the potential of designing or identifying differential inhibitors of P. falciparum and mammalian prenyl transferases as an approach to novel malaria therapy.

IT 175520-18-0, L 745631
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protein farnesyltransferase inhibitor; protein prenyltransferase activities of Plasmodium falciparum)

RN 175520-18-0 CAPLUS

CN 1-Piperazinepropanethiol, β-amino-2-(2-methoxyethyl)-4-(1-naphthalenylcarbonyl)-, (βR,2S)- (9CI) (CA INDEX NAME)

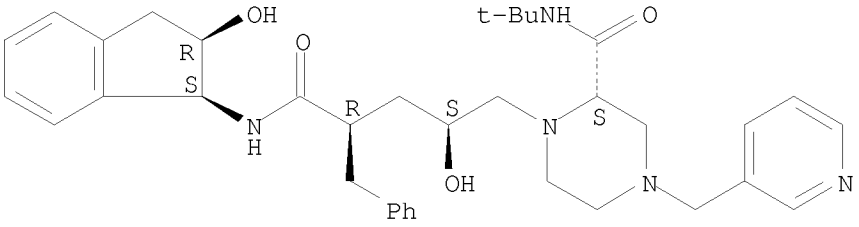
Absolute stereochemistry.



RE.CNT 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

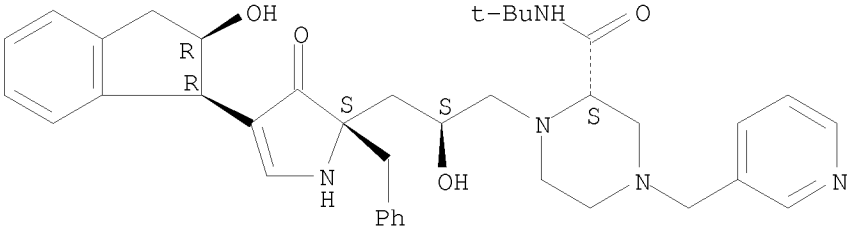
L8 ANSWER 19 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1998:331224 CAPLUS
DN 129:75969
TI Transport characteristics of peptidomimetics. Effect of the pyrrolinone bioisostere on transport across Caco-2 cell monolayers
AU Sudoh, Masao; Pauletti, Giovanni M.; Yao, Wenqing; Moser, William; Yokoyama, Akihisa; Pasternak, Alexander; Sprengeler, Paul A.; Smith, Amos B., III; Hirschmann, Ralph; Borchardt, Ronald T.
CS Department of Pharmaceutical Chemistry, The University of Kansas, Lawrence, KS, 66047, USA
SO Pharmaceutical Research (1998), 15(5), 719-725
CODEN: PHREEB; ISSN: 0724-8741
PB Plenum Publishing Corp.
DT Journal
LA English
AB To compare the permeation characteristics of amide bond-containing HIV-1 protease inhibitors and their pyrrolinone-containing counterparts across Caco-2 cell monolayers, a model of the intestinal mucosa. Transepithelial transport and cellular uptake of three pairs of amide bond-containing and pyrrolinone-based peptidomimetics were assessed in the presence and absence of cyclosporin A using the Caco-2 cell culture model. The potential of the peptidomimetics to interact with biol. membranes was estimated by IAM chromatog. In the absence of cyclosporin A, apical (AP) to basolateral (BL) flux of all compds. studied was less than the flux determined in the opposite direction (i.e., BL-to-AP). The ratio of the apparent permeability coeffs. (Papp) calculated for the BL-to-AP and AP-to-BL transport (PBL→AP/PAP→BL) varied between 1.7 and 36.2. When individual pairs were compared, PBL→AP/PAP→BL ratios of the pyrrolinone-containing compds. were 1.5 to 11.5 times greater than those determined for the amide bond-containing analogs. Addition of 25 μM cyclosporin A to the transport buffer reduced the PBL→AP/PAP→BL ratios for all protease inhibitors to a value close to unity. Under these conditions, the amide bond-containing peptidomimetics were at least 1.6 to 2.8 times more able to permeate Caco-2 cell monolayers than were the pyrrolinone-containing compds. The intrinsic uptake characteristics into Caco-2 cells determined in the presence of 25 μM cyclosporin A were slightly greater for the amide bond-containing protease inhibitors than for the pyrrolinone-containing analogs. These uptake results are consistent with the transepithelial transport results determined across this in vitro model of the intestinal mucosa.
IT 150378-17-9 192799-04-5
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(transport characteristics of peptidomimetics across Caco-2 cell monolayers as intestinal mucosa model and effect cyclosporin A in relation to pyrrolinone bioisostere)
RN 150378-17-9 CAPLUS
CN D-erythro-Pentonamide, 2,3,5-trideoxy-N-[(1S,2R)-2,3-dihydro-2-hydroxy-1H-inden-1-yl]-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)- (CA INDEX NAME)

Absolute stereochemistry.



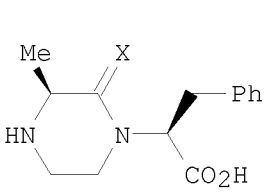
RN 192799-04-5 CAPLUS
CN 2-Piperazinecarboxamide, 1-[(2S)-3-[(2S)-4-[(1R,2R)-2,3-dihydro-2-hydroxy-1H-inden-1-yl]-2,3-dihydro-3-oxo-2-(phenylmethyl)-1H-pyrrol-2-yl]-2-hydroxypropyl]-N-(1,1-dimethylethyl)-4-(3-pyridinylmethyl)-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

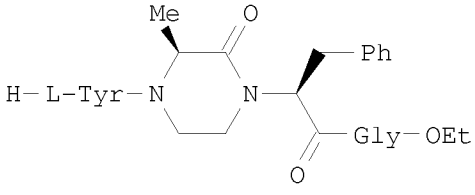


RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 20 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1998:5383 CAPLUS
DN 128:102361
TI Synthesis and opiate activity of pseudo-tetrapeptides containing chiral piperazin-2-one and piperazine derivatives
AU Yamashita, Tetsushi; Tsuru, Eiji; Banjyo, Eri; Doe, Matsumi; Shibata, Kozo; Yasuda, Masahide; Gemba, Munekazu
CS Department of Chemistry, Faculty of Science, Osaka City University, Osaka, 558, Japan
SO Chemical & Pharmaceutical Bulletin (1997), 45(12), 1940-1944
CODEN: CPBTAL; ISSN: 0009-2363
PB Pharmaceutical Society of Japan
DT Journal
LA English
GI



I



II

AB Enantiomeric piperazin-2-one derivs., N,N'-ethylene-bridged alanylphenylalanines, e.g. I (X = O), were prepared using L- or D-Ala and L- or D-Phe as starting materials, and were inserted into the second and

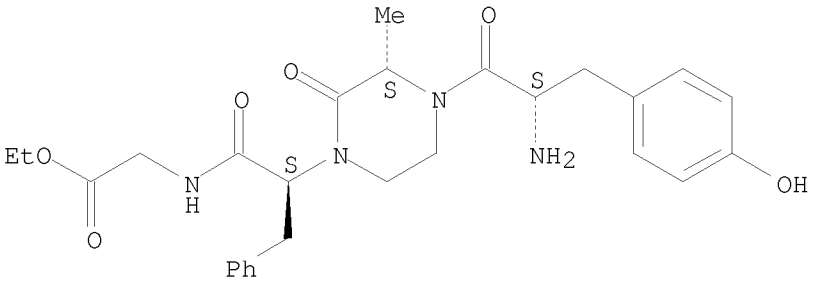
third positions of enantiomeric pseudotetrapeptides, e.g. II. The corresponding piperazine derivs., e.g. I (X = H2) were obtained by selective BH3 reduction of the amide carbonyl groups and similarly inserted into the same positions of the tetrapeptides. Enantiomeric N,N'-ethylene-bridged Tyr-Tyr derivs., obtained from L- or D-Tyr, were also inserted into the first and second positions of two pairs of enantiomeric tetrapeptides. The opiate activities of the 8 peptides thus obtained were studied by use of the mouse vas deferens and the guinea pig ileum assays in order to elucidate the structure-activity relationships of these peptides, especially with respect to stereochem.

IT 201293-48-3P 201293-49-4P 201293-55-2P
201293-56-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and opiate activity of pseudotetrapeptides containing chiral piperazinone and piperazine derivs.)

RN 201293-48-3 CAPLUS

CN Glycine, L-tyrosyl-(αS,3S)-3-methyl-2-oxo-α-(phenylmethyl)-1-piperazineacetyl-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

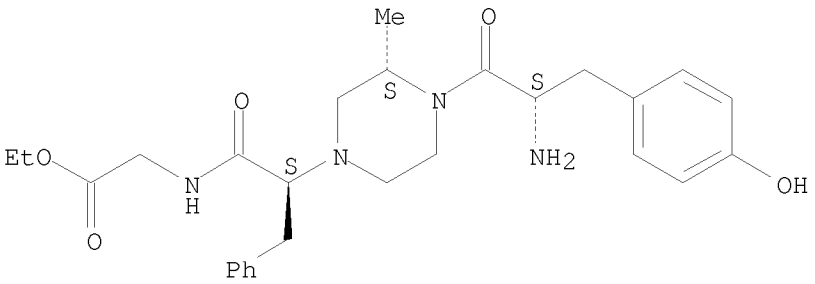


● HCl

RN 201293-49-4 CAPLUS

CN Glycine, L-tyrosyl-(αS,3S)-3-methyl-α-(phenylmethyl)-1-piperazineacetyl-, ethyl ester, dihydrochloride (9CI) (CA INDEX NAME)

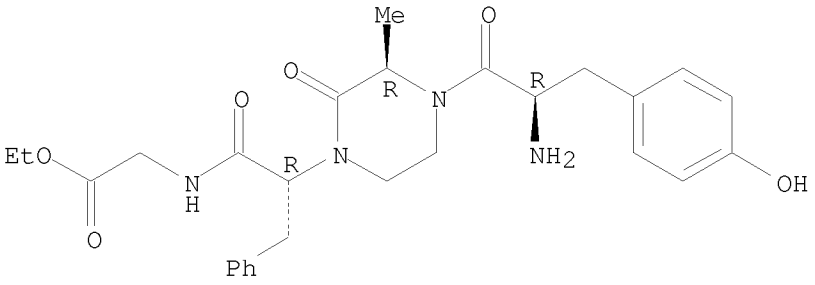
Absolute stereochemistry. Rotation (-).



●2 HCl

RN 201293-55-2 CAPLUS
CN Glycine, D-tyrosyl-(αR,3R)-3-methyl-2-oxo-α-(phenylmethyl)-1-piperazineacetyl-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

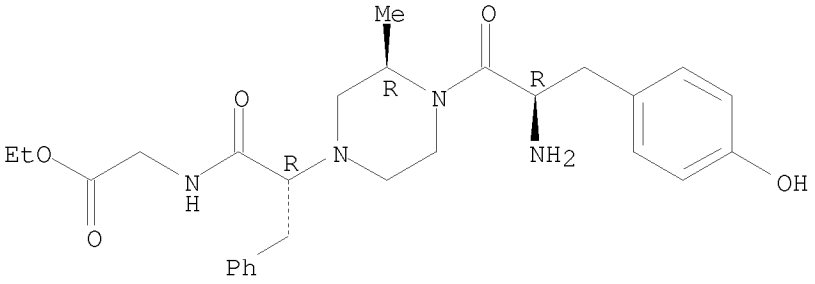
Absolute stereochemistry. Rotation (+).



● HCl

RN 201293-56-3 CAPLUS
CN Glycine, D-tyrosyl-(αR,3R)-3-methyl-α-(phenylmethyl)-1-piperazineacetyl-, ethyl ester, dihydrochloride (9CI) (CA INDEX NAME)

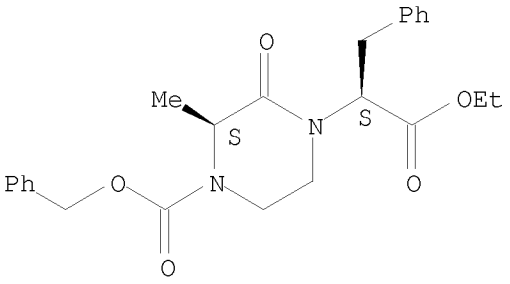
Absolute stereochemistry. Rotation (+).



●2 HCl

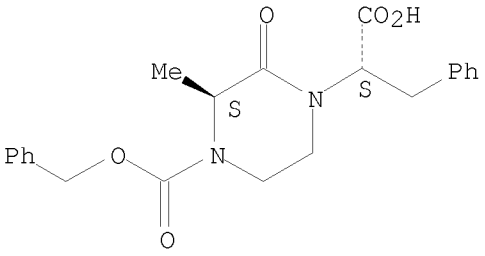
IT 201293-41-6P 201293-42-7P 201293-43-8P
201293-45-0P 201293-47-2P 201293-50-7P
201293-51-8P 201414-33-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and opiate activity of pseudotetrapeptides containing chiral piperazinone and piperazine derivs.)
RN 201293-41-6 CAPLUS
CN 1-Piperazineacetic acid, 3-methyl-2-oxo-4-[(phenylmethoxy)carbonyl]-α-(phenylmethyl)-, ethyl ester, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



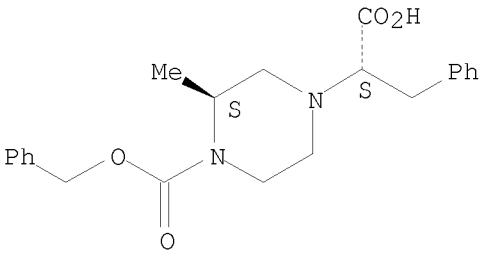
RN 201293-42-7 CAPLUS
CN 1-Piperazineacetic acid, 3-methyl-2-oxo-4-[(phenylmethoxy)carbonyl]-α-(phenylmethyl)-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



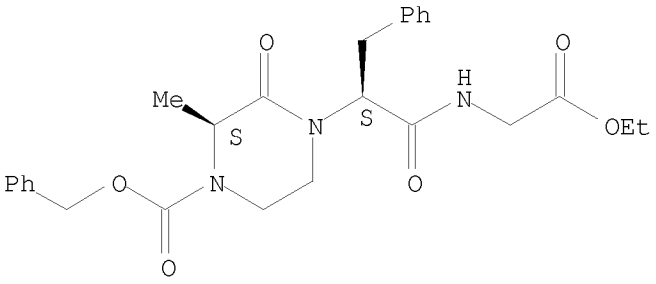
RN 201293-43-8 CAPLUS
CN 1-Piperazineacetic acid, 3-methyl-4-[(phenylmethoxy)carbonyl]-α-(phenylmethyl)-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



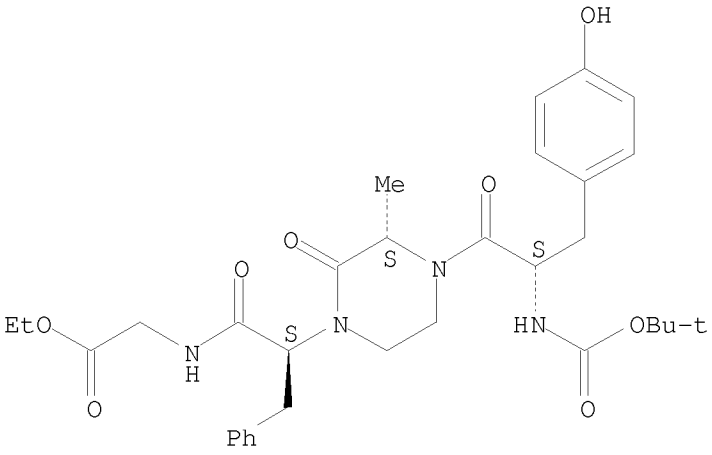
RN 201293-45-0 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[2-[(2-ethoxy-2-oxoethyl)amino]-2-oxo-1-(phenylmethyl)ethyl]-2-methyl-3-oxo-, phenylmethyl ester, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



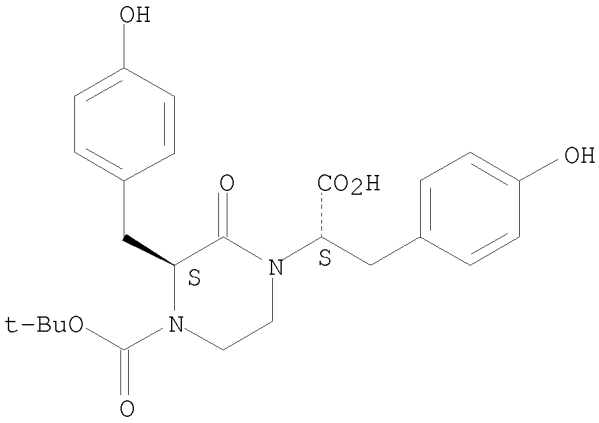
RN 201293-47-2 CAPLUS
CN Glycine, N-[(1,1-dimethylethoxy)carbonyl]-L-tyrosyl-(αS,3S)-3-methyl-2-oxo-α-(phenylmethyl)-1-piperazineacetyl-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 201293-50-7 CAPLUS
CN 1-Piperazineacetic acid, 4-[(1,1-dimethylethoxy)carbonyl]-α,3-bis[(4-hydroxyphenyl)methyl]-2-oxo-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

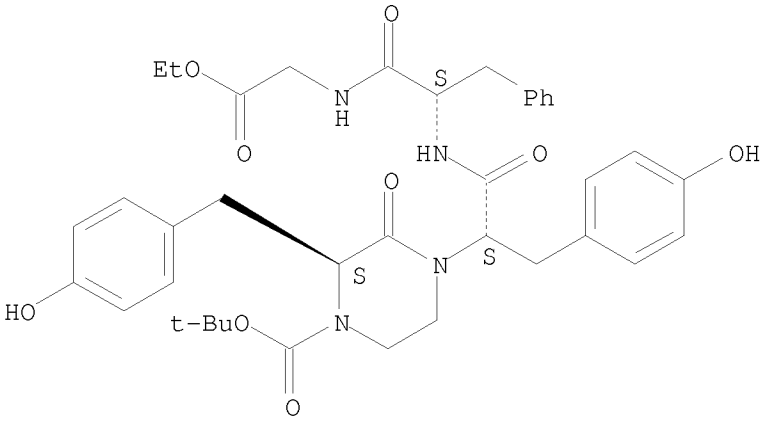
Absolute stereochemistry. Rotation (-).



RN 201293-51-8 CAPLUS

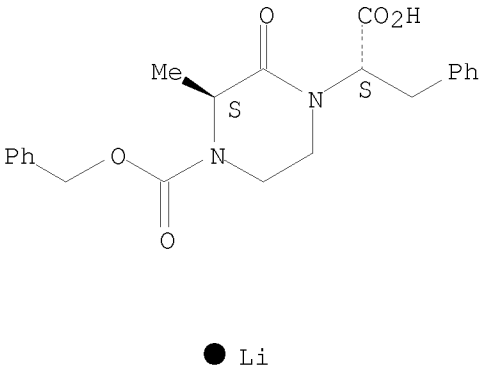
CN Glycine, N-[(2S)-2-[(3S)-4-[(1,1-dimethylethoxy)carbonyl]-3-[(4-hydroxyphenyl)methyl]-2-oxo-1-piperazinyl]-3-(4-hydroxyphenyl)-1-oxopropyl]-L-phenylalanyl-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 201414-33-7 CAPLUS
CN 1-Piperazineacetic acid, 3-methyl-2-oxo-4-[(phenylmethoxy)carbonyl]-α-(phenylmethyl)-, lithium salt, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● Li

RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 21 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1997:740109 CAPLUS
DN 128:13146
TI Preparation of norbornene-containing peptide analogs as HIV protease inhibitors useful for the treatment of AIDS
IN Hungate, Randall W.; Kim, Byeong Moon; Vacca, Joseph P.
PA Kim, Byeong Moon, USA; Vacca, Joseph P.; Merck & Co., Inc.; Hungate, Randall W.
SO PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

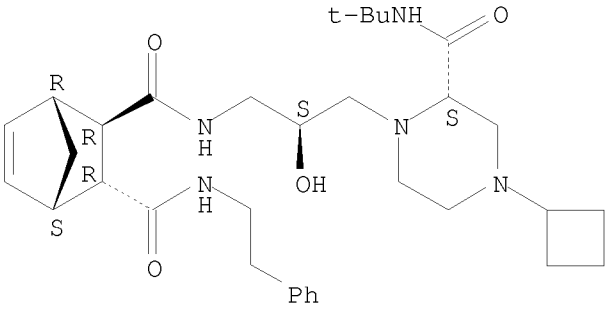
PI WO 9740825 A1 19971106 WO 1997-US6595 19970429
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
US 1996-16685P P 19960502
GB 1996-13488 A 19960627
CA 2252918 A1 19971106 CA 1997-2252918 19970429
US 1996-16685P P 19960502
GB 1996-13488 A 19960627
AU 9729238 A 19971119 AU 1997-29238 19970429
AU 711713 B2 19991021
US 1996-16685P P 19960502
GB 1996-13488 A 19960627
WO 1997-US6595 W 19970429
EP 912170 A1 19990506 EP 1997-923431 19970429
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI
US 1996-16685P P 19960502
GB 1996-13488 A 19960627
WO 1997-US6595 W 19970429
JP 2000509389 T 20000725 JP 1997-538974 19970429
US 1996-16685P P 19960502
GB 1996-13488 A 19960627
WO 1997-US6595 W 19970429
OS MARPAT 128:13146
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I and II [R, R1 = independently H, (un)substituted C3-5 cycloalkyl, (un)substituted aryl, C1-4 alkyl (un)substituted with halo, OH, C1-3 alkoxy, (un)substituted aryl, W-aryl, W-benzyl, (un)substituted heterocycle, CO2H; W = O, S, NH; RR1 form 4-6 membered ring; R2 = H, (un)substituted Ph, (un)substituted C5-7 cycloalkyl, C1-4 alkyl; R3 = CH2NR5R6, fragment X; R4 = (un)substituted 5-7-membered heterocycle, (un)substituted aryl, (un)substituted C1-4 alkyl, (un)substituted C3-5 cycloalkyl; R5 = VR4; V = COQ, SO2Q; Q = bond, O, NH; R6 = H, (un)substituted C1-4 alkyl, (un)substituted C3-5 cycloalkyl, (un)substituted aryl; J = any group Q1-Q3], and pharmaceutically acceptable salts thereof, are HIV protease inhibitors. These compds. are useful in the prevention or treatment of infection by HIV and in the treatment of AIDS, either as compds., pharmaceutically acceptable salts, pharmaceutical composition ingredients, whether or not in combination with other antivirals, immunomodulators, antibiotics or vaccines. Methods of treating AIDS and methods of preventing or treating infection by HIV are also described. Thus, amidation of norbornene III (preparation given) with indane-containing peptide mimic IV (preparation given) gave 39% norbornene pentaneamide V. Prepared compound V inhibited microbial expressed HIV protease with IC50 = 0.055 nM.
IT 198972-95-1P 198972-96-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of norbornene-containing peptide analogs as HIV protease inhibitors useful for the treatment of AIDS)
RN 198972-95-1 CAPLUS

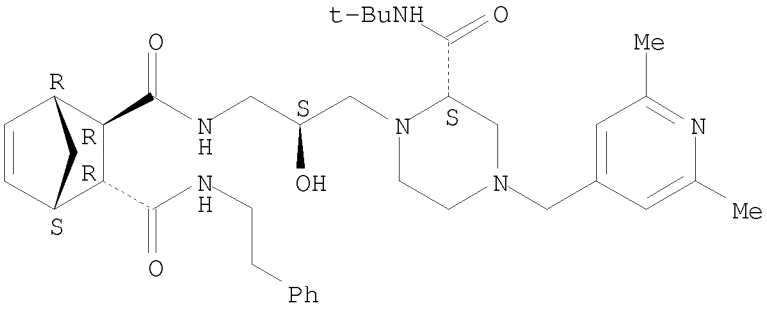
CN Bicyclo[2.2.1]hept-5-ene-2,3-dicarboxamide, N-[(2S)-3-[(2S)-4-cyclobutyl-2-[[(1,1-dimethylethyl)amino]carbonyl]-1-piperazinyl]-2-hydroxypropyl]-N'-(2-phenylethyl)-, (1R,2R,3R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 198972-96-2 CAPLUS
CN Bicyclo[2.2.1]hept-5-ene-2,3-dicarboxamide, N-[(2S)-3-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-[(2,6-dimethyl-4-pyridinyl)methyl]-1-piperazinyl]-2-hydroxypropyl]-N'-(2-phenylethyl)-, (1R,2R,3R,4S)- (9CI) (CA INDEX NAME)

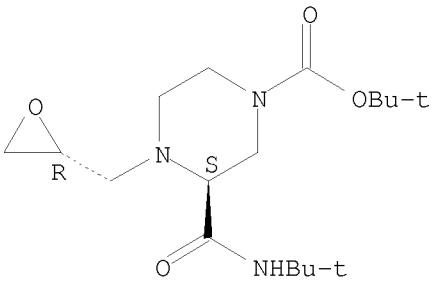
Absolute stereochemistry.



IT 158380-45-1P 198972-91-7P 198972-92-8P
198972-93-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of norbornene-containing peptide analogs as HIV protease inhibitors useful for the treatment of AIDS)

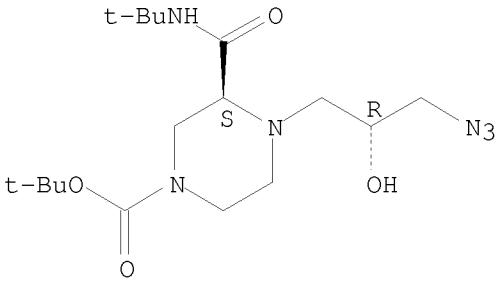
RN 158380-45-1 CAPLUS
CN 1-Piperazinecarboxylic acid, 3-[[(1,1-dimethylethyl)amino]carbonyl]-4-[(2R)-oxiranylmethyl]-, 1,1-dimethylethyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



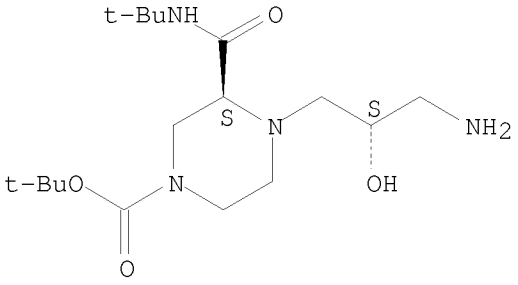
RN 198972-91-7 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[(2R)-3-azido-2-hydroxypropyl]-3-[[(1,1-dimethylethyl)amino]carbonyl]-, 1,1-dimethylethyl ester, (3S)- (CA INDEX NAME)

Absolute stereochemistry.



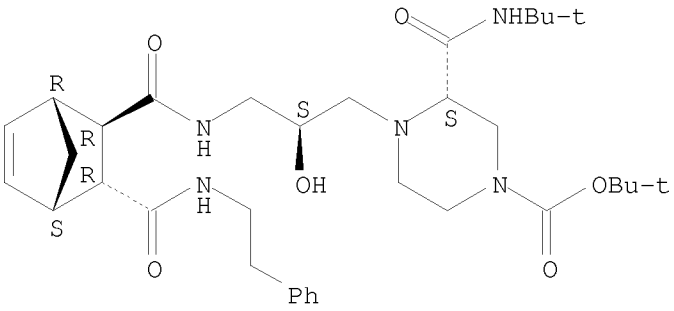
RN 198972-92-8 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[(2S)-3-amino-2-hydroxypropyl]-3-[[(1,1-dimethylethyl)amino]carbonyl]-, 1,1-dimethylethyl ester, (3S)- (CA INDEX NAME)

Absolute stereochemistry.



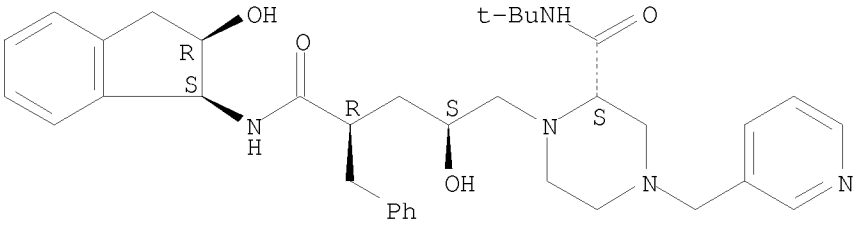
RN 198972-93-9 CAPLUS
CN 1-Piperazinecarboxylic acid, 3-[[(1,1-dimethylethyl)amino]carbonyl]-4-[(2S)-2-hydroxy-3-[[[(1R,2R,3R,4S)-3-[[(2-phenylethyl)amino]carbonyl]bicyclo[2.2.1]hept-5-en-2-yl]carbonyl]amino]propyl]-, 1,1-dimethylethyl ester, (3S)- (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 22 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1997:156459 CAPLUS
DN 126:258416
TI Pharmacokinetic enhancement of inhibitors of the human immunodeficiency virus protease by coadministration with ritonavir
AU Kempf, Dale J.; Marsh, Kennan C.; Kumar, Gondi; Rodrigues, A. David; Denissen, Jon F.; McDonald, Edith; Kukulka, Michael J.; Hsu, Ann; Granneman, G. Richard; Baroldi, Paolo A.; Sun, Eugene; Pizzuti, David; Plattner, Jacob J.; Norbeck, Daniel W.; Leonard, John M.
CS Dep. Infectious Diseases Res., Abbott Lab., Abbott Park, IL, 60064, USA
SO Antimicrobial Agents and Chemotherapy (1997), 41(3), 654-660
CODEN: AMACCQ; ISSN: 0066-4804
PB American Society for Microbiology
DT Journal
LA English
AB Coadministration with the human immunodeficiency virus (HIV) protease inhibitor ritonavir was investigated as a method for enhancing the levels of other peptidomimetic HIV protease inhibitors in plasma. In rat and human liver microsomes, ritonavir potently inhibited the cytochrome P 450 (CYP)-mediated metabolism of saquinavir, indinavir, nelfinavir, and VX-478. The structural features of ritonavir responsible for CYP binding and inhibition were examined Coadministration of other protease inhibitors with ritonavir in rats and dogs produced elevated and sustained plasma drug levels 8 to 12 h after a single dose. Drug exposure in rats was elevated by 8- to 46-fold. A >50-fold enhancement of the concns. of saquinavir in plasma was observed in humans following a single co-dose of ritonavir (600 mg) and saquinavir (200 mg). These results indicate that ritonavir can favorably alter the pharmacokinetic profiles of other protease inhibitors. Combination regimens of ritonavir and other protease inhibitors may thus play a role in the treatment of HIV infection. Because of potentially substantial drug level increases, however, such combinations require further investigation to establish safe regimens for clin. use.
IT 150378-17-9, Indinavir
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pharmacokinetic enhancement of inhibitors of human immunodeficiency virus protease by coadministration with ritonavir in relation to metabolism by cytochrome P 450)
RN 150378-17-9 CAPLUS
CN D-erythro-Pentonamide, 2,3,5-trideoxy-N-[(1S,2R)-2,3-dihydro-2-hydroxy-1H-inden-1-yl]-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)- (CA INDEX NAME)

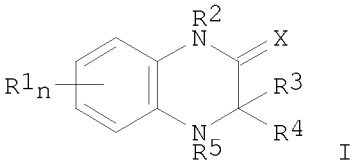
Absolute stereochemistry.



L8 ANSWER 23 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1996:601709 CAPLUS
DN 125:238651
TI Use of quinoxalines and protease inhibitors in a composition for the treatment of AIDS and/or HIV infections
IN Paessens, Arnold; Blunck, Martin; Riess, Guenther; Kleim, Joerg-Peter; Roesner, Manfred
PA Bayer A.-G., Germany
SO Eur. Pat. Appl., 24 pp.
CODEN: EPXXDW
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
PI EP 728481	A2	19960828	EP 1996-102129		19960214
EP 728481	A3	19980708			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
			DE 1995-19506742	A	19950227
DE 19506742	A1	19960829	DE 1995-19506742		19950227
AU 9645615	A	19960905	AU 1996-45615		19960220
AU 710158	B2	19990916			
			DE 1995-19506742	A	19950227
CA 2170222	A1	19960828	CA 1996-2170222		19960223
			DE 1995-19506742	A	19950227
FI 9600850	A	19960828	FI 1996-850		19960223
			DE 1995-19506742	A	19950227
JP 08245392	A	19960924	JP 1996-60286		19960223
			DE 1995-19506742	A	19950227
IL 117247	A	20001031	IL 1996-117247		19960223
			DE 1995-19506742	A	19950227
NO 9600775	A	19960828	NO 1996-775		19960226
			DE 1995-19506742	A	19950227
ZA 9601516	A	19960903	ZA 1996-1516		19960226
			DE 1995-19506742	A	19950227
HU 9600455	A2	19961230	HU 1996-455		19960226
HU 9600455	A3	19980428			
			DE 1995-19506742	A	19950227
BR 9600809	A	19971223	BR 1996-809		19960226
			DE 1995-19506742	A	19950227
CN 1141196	A	19970129	CN 1996-102709		19960227
			DE 1995-19506742	A	19950227

OS MARPAT 125:238651
GI



I

AB Combinations of a quinoxaline derivative [I; R1 = halo, OH, NO2, (substituted) amino, N3, CF3, CF3O, C1-8 alkyl, CN, (substituted) Ph, N-heterocyclyl, etc.; R2, R5 = H, OH, C1-6 alkoxy, aryloxy, C1-6 acyloxy, CN, (substituted) amino, (substituted) C1-8 alkyl, (substituted) C2-8 alkenyl, (substituted) C3-8 alkynyl, (substituted) C3-8 cycloalk(en)yl, etc.; R3, R4 = H, (substituted) C1-8 alkyl, (substituted) C2-8 alkenyl, (substituted) C3-8 cycloalk(en)yl, (substituted)aryl, etc.; or R3R4 or R3R5 complete a (substituted) ring; X = O, S, Se, NR2; n = 0-4] and a peptidomimetic protease inhibitor are useful for treatment of HIV infections and AIDS. Thus, I [R1 = 6-MeO, R2 = R3 = H, R4 = (S)-MeSCH2, R5 = i-PrO2C, X = S] (0.7-6 nM) and saquinavir (6-50 nM) synergistically inhibited syncytium formation in HIV-infected human lymphocytes in vitro.

IT 157810-81-6, L 735524
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of quinoxalines and protease inhibitors for treatment of AIDS and HIV infections)

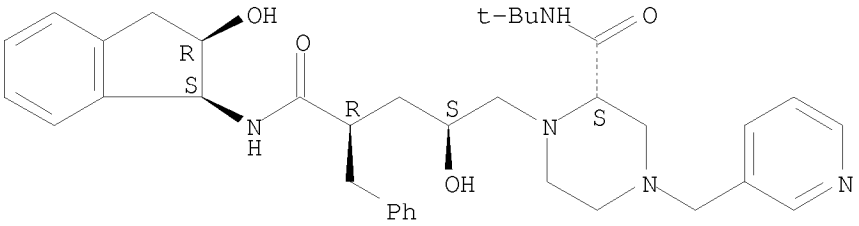
RN 157810-81-6 CAPLUS

CN D-erythro-Pentonamide, 2,3,5-trideoxy-N-[(1S,2R)-2,3-dihydro-2-hydroxy-1H-inden-1-yl]-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)-, sulfate (1:1) (CA INDEX NAME)

CM 1

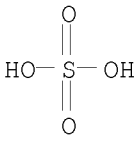
CRN 150378-17-9
CMF C36 H47 N5 O4

Absolute stereochemistry.



CM 2

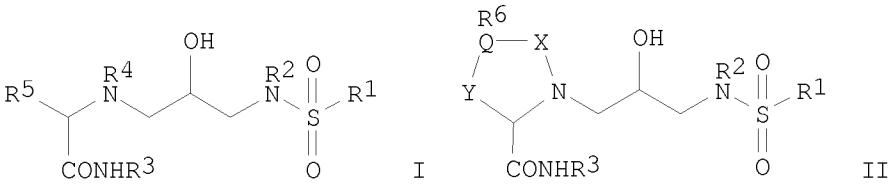
CRN 7664-93-9
CMF H2 O4 S



L8 ANSWER 24 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1996:366115 CAPLUS
DN 125:115158
TI Peptidomimetic N-(2-hydroxy-3-aminopropyl)sulfonamides as proteolytic enzyme inhibitors
IN Sprengeler, Paul; Smith, Amos B., III; Hirschmann, Ralph F.; Yokoyama, Akihisa
PA University of Pennsylvania, USA
SO U.S., 9 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5519060	A	19960521	US 1995-373564	19950117
WO 9622087	A1	19960725	WO 1996-US501	19960116
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
			US 1995-373564 A	19950117

OS MARPAT 125:115158
GI

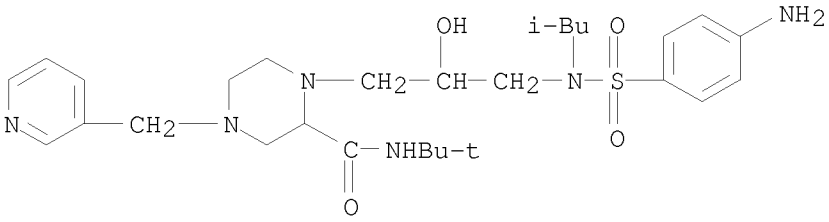


AB A method is claimed for modulating the activity of an enzyme (no data), comprising contacting said enzyme with at least one compound having structure I or II: wherein: R1 is H, OH, alkyl having 1 to about 10 carbon atoms, or aryl having 3 to about 20 carbon atoms; R2 is H, alkyl having 1 to about 10 carbon atoms, aryl having 3 to about 20 carbon atoms, alkaryl having 4 to about 25 carbon atoms, or an amino acid side chain; R3 is H, alkyl having one to about 10 carbon atoms, or alkaryl having 4 to about 25 carbon atoms; R4 is H, alkyl having 1 to about 10 carbon atoms, aryl having 3 to about 20 carbon atoms, alkaryl having 4 to about 25 carbon atoms, or an amino acid side chain; R5 is H, alkyl having one to about 10 carbon atoms, or aryl having 3 to about 20 carbon atoms; R6 is H, alkyl having one to about 10 carbon atoms, aryl having 3 to about 20 carbon atoms, or alkaryl having 4 to about 25 carbon atoms; X and Y are, independently, alkylene having 1 to about 6 carbon atoms, provided that the sum of X and Y is less than or equal to 9; and Q is N or CH2. Synthetic schemes for the preparation of representative II structures are provided.
IT 178942-68-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(peptidomimetic N-(2-hydroxy-3-aminopropyl)sulfonamides as proteolytic enzyme inhibitors)

RN 178942-68-2 CAPLUS

CN 2-Piperazinecarboxamide, 1-[3-[[(4-aminophenyl)sulfonyl](2-methylpropyl)amino]-2-hydroxypropyl]-N-(1,1-dimethylethyl)-4-(3-pyridinylmethyl)- (CA INDEX NAME)



=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	220.92	400.87

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-38.40	-38.40

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FULL ESTIMATED COST	3.30	404.17

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CA SUBSCRIBER PRICE	0.00	-38.40

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                  custom IPC display formats
 NEWS  5  JAN 28  MARPAT searching enhanced
 NEWS  6  JAN 28  USGENE now provides USPTO sequence data within 3 days
                  of publication
 NEWS  7  JAN 28  TOXCENTER enhanced with reloaded MEDLINE segment
 NEWS  8  JAN 28  MEDLINE and LMEDLINE reloaded with enhancements
 NEWS  9  FEB 08  STN Express, Version 8.3, now available
 NEWS 10  FEB 20  PCI now available as a replacement to DPCI
 NEWS 11  FEB 25  IFIREF reloaded with enhancements
 NEWS 12  FEB 25  IMSPRODUCT reloaded with enhancements
 NEWS 13  FEB 29  WPINDEX/WPIDS/WPIX enhanced with ECLA and current
                  U.S. National Patent Classification
 NEWS 14  MAR 31  IFICDB, IFIPAT, and IFIUDB enhanced with new custom
                  IPC display formats
 NEWS 15  MAR 31  CAS REGISTRY enhanced with additional experimental
                  spectra
 NEWS 16  MAR 31  CA/CAplus and CASREACT patent number format for U.S.
                  applications updated
 NEWS 17  MAR 31  LPCI now available as a replacement to LDPCI
 NEWS 18  MAR 31  EMBASE, EMBAL, and LEMBASE reloaded with enhancements
 NEWS 19  APR 04  STN AnaVist, Version 1, to be discontinued

 NEWS EXPRESS FEBRUARY 08 CURRENT WINDOWS VERSION IS V8.3,
              AND CURRENT DISCOVER FILE IS DATED 20 FEBRUARY 2008

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                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

FILE 'MEDLINE' ENTERED AT 11:07:34 ON 09 APR 2008

FILE 'BIOSIS' ENTERED AT 11:07:34 ON 09 APR 2008
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FILE 'SCISEARCH' ENTERED AT 11:07:34 ON 09 APR 2008

FILE 'EMBASE' ENTERED AT 11:07:34 ON 09 APR 2008

FILE 'WPIDS' ENTERED AT 11:07:34 ON 09 APR 2008

=> melanocortin (s) receptor and (treat or treat? or therap?)
L1 3147 MELANOCORTIN (S) RECEPTOR AND (TREAT OR TREAT? OR THERAP?)

=> petidomimetic and l1
L2 0 PETIDOMIMETIC AND L1

=> peptidomimetic and l1
L3 19 PEPTIDOMIMETIC AND L1

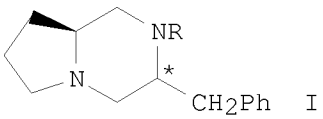
=> dup rem l3
PROCESSING COMPLETED FOR L3
L4 12 DUP REM L3 (7 DUPLICATES REMOVED)

=> d ibib abs l4 1-12

L4 ANSWER 1 OF 12 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2008210394 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 18220330
TITLE: Backbone cyclic peptidomimetic melanocortin-4 receptor agonist as a novel orally administrated drug lead for treating obesity.
AUTHOR: Hess Shmuel; Linde Yaniv; Ovadia Oded; Safrai Eli; Shalev Deborah E; Swed Avi; Halbfinger Efrat; Lapidot Tair; Winkler Ilan; Gabinet Yael; Faier Avi; Yarden Dana; Xiang Zhimin; Portillo Federico P; Haskell-Luevano Carrie; Gilon Chaim; Hoffman Amnon
CORPORATE SOURCE: Department of Pharmaceutics, School of Pharmacy, The Hebrew University of Jerusalem, Jerusalem 91120, Israel.
SOURCE: Journal of medicinal chemistry, (2008 Feb 28) Vol. 51, No. 4, pp. 1026-34. Electronic Publication: 2008-01-26. Journal code: 9716531. ISSN: 0022-2623.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: NONMEDLINE; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 29 Mar 2008
Last Updated on STN: 29 Mar 2008
AB The tetrapeptide sequence His-Phe-Arg-Trp, derived from melanocyte-stimulating hormone (alphaMSH) and its analogs, causes a decrease in food intake and elevates energy utilization upon binding to the melanocortin-4 receptor (MC4R). To utilize this sequence as an effective agent for treating obesity, we improved its metabolic stability and intestinal permeability by synthesizing a library of backbone cyclic peptidomimetic derivatives. One analog, peptide 1 (BL3020-1), was selected according to its selectivity in activating the MC4R, its favorable transcellular penetration through

enterocytes and its enhanced intestinal metabolic stability. This peptide was detected in the brain following oral administration to rats. A single oral dose of 0.5 mg/kg in mice led to reduced food consumption (up to 48% vs the control group) that lasted for 5 h. Repetitive once daily oral dosing (0.5 mg/kg/day) for 12 days reduced weight gain. Backbone cyclization was shown to produce a potential drug lead for treating obesity.

L4 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:934985 CAPLUS
DOCUMENT NUMBER: 145:489153
TITLE: Design, synthesis, and biological evaluation of a new class of small molecule peptide mimetics targeting the melanocortin receptors
AUTHOR(S): Cain, James P.; Mayorov, Alexander V.; Cai, Minying; Wang, Hui; Tan, Bahar; Chandler, Kevin; Lee, YeonSun; Petrov, Ravil R.; Trivedi, Dev; Hruby, Victor J.
CORPORATE SOURCE: Department of Chemistry, University of Arizona, Tucson, AZ, 85721, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(20), 5462-5467
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 145:489153
GI



I

AB A new bicyclic template has been developed for the synthesis of peptidomimetics. Straightforward synthetic steps, starting from proline and phenylalanine, allow the synthesis of a wide range of bicyclic peptidomimetics I [R = COCH2Ph, CO(CH2)2CONH(CH2)2-3-indolyl, CO(CH2)2-3-indolyl, CO(CH2)5NHCO(CH2)2-3-indolyl, argininyl-CO(CH2)2-3-indolyl; * indicates that both R and S diastereomers were prepared for some of the compds.]. This system was designed to target the melanocortin receptors (MCRs), with functional group selection based on a known pharmacophore and guidance from mol. modeling to rationally identify positional and stereochem. isomers likely to be active. The functions of hMCRs are critical to myriad of biol. activities, including pigmentation, steroidogenesis, energy homeostasis, erectile activity, and inflammation. These G-protein-coupled receptors (GPCRs) are targets for drug discovery in a number of areas, including cancer, pain, and obesity therapeutics. All compds. from this series tested to date are antagonists which bind with high affinity. Importantly, many are highly selective for a particular MCR subtype, including some of the first completely hMC5R-selective antagonists reported.
REFERENCE COUNT: 122 THERE ARE 122 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:425889 CAPLUS
DOCUMENT NUMBER: 144:481641
TITLE: Melanocortin metallopeptide constructs, combinatorial

libraries, and therapeutic applications
INVENTOR(S): Cai, Hui-Zhi; Yang, Wei; Shi, Yi-Qun; Sharma, Shubh D.
PATENT ASSIGNEE(S): Palatin Technologies, Inc., USA
SOURCE: Aust. Pat. Appl., 81 pp.
CODEN: AUXXCM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
AU 2005201166	A1	20050505	AU 2005-201166	20050317
PRIORITY APPLN. INFO.:			AU 2000-58742 A3	20000615

AB The present invention relates to metallopeptides, metal ion-complexed peptidomimetics, and metallo-constructs, including metallopeptide combinatorial libraries, metal ion-complexed peptidomimetic and peptide-like combinatorial libraries and metallo-construct combinatorial libraries, specific for melanocortin receptors, including methods for the use and making of the same. The invention also relates to methods for synthesizing and assembling such libraries, and methods for identification and characterization of library constituents which are capable of binding a melanocortin receptor of interest, or mediating a melanocortin receptor-related biol. activity of interest. Metallopeptides of this invention that are melanocortin receptor 1 specific can be used as radiodiagnostic agents or radiotherapeutic agents when complexed to radionuclides. Metallopeptides of this invention that are melanocortin receptor 1 specific can be used as chemopreventive agents against sun-induced neoplastic activity in human skin. Metallopeptides of this invention that are melanocortin receptor 4 antagonists can also be used as a therapeutic agent in eating disorders.

L4 ANSWER 4 OF 12 EMBASE
ACCESSION NUMBER: 2005014275 EMBASE
TITLE: The MC(4) receptor as a therapeutic target.
AUTHOR: Chaki, Shigeyuki (correspondence); Nakazato, Atsuro
CORPORATE SOURCE: Medicinal Research Laboratories, Taisho Pharmaceutical Co., Ltd., 1-403 Yoshino-cho, Kita-ku, Saitama, Saitama 331-9530, Japan. s.chaki@po.rd.taisho.co.jp
SOURCE: Drugs of the Future, (Oct 2004) Vol. 29, No. 10, pp. 1065-1074.
Refs: 91
ISSN: 0377-8282 CODEN: DRFUD4
COUNTRY: Spain
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 003 Endocrinology
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 27 Jan 2005
Last Updated on STN: 27 Jan 2005

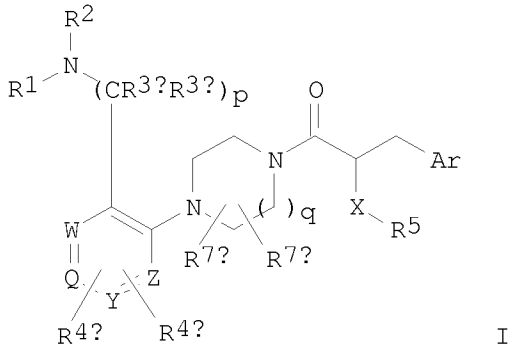
AB Melanocortins, which are derived from pro-opiomelanocortin (POMC) by enzymatic processing, are involved in a wide range of physiological events. The melanocortins exert their effects by binding to melanocortin receptors. To date, five receptor subtypes, MC(1)-MC(5), all of which are G-protein-coupled receptors, have been cloned. Of these, the MC(4) receptor, the expression of which is restricted to the central nervous system (CNS), is of interest in terms of the central regulation of feeding behavior and energy homeostasis. Recent findings on the distribution of

the receptor in the brain and studies with selective agonists/antagonists have underscored its role in stress responses, the development of addiction, nociception and sexual function. The MC(4) receptor may therefore be an attractive target for the treatment of many CNS-related disorders, such as obesity, cachexia, depression/anxiety, drug addiction, pain and sexual dysfunction.

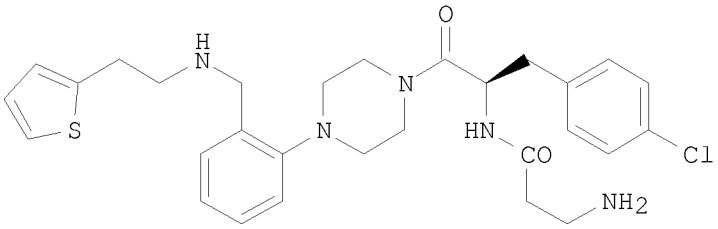
L4 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:913002 CAPLUS
DOCUMENT NUMBER: 139:395952
TITLE: Substituted piperazine derivatives as melanocortin receptor ligands, and their preparation, pharmaceutical compositions, and use
INVENTOR(S): Pontillo, Joseph; Marinkovic, Dragan; Lanier, Marion C.; Tran Joe Ahn; Arellano, Melissa; Parker, Jessica; Nelson, Jodie; Chen, Chen; Chen, Caroline; Jiang, Wanglong; White, Nicole; Tucci, Fabio C.
PATENT ASSIGNEE(S): Neurocrine Biosciences, Inc., USA
SOURCE: PCT Int. Appl., 153 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003094918	A1	20031120	WO 2003-US14628		20030509
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2003230367	A1	20031111	AU 2003-230367		20030509
CA 2484968	A1	20031120	CA 2003-2484968		20030509
US 20040053933	A1	20040318	US 2003-434803		20030509
EP 1503761	A1	20050209	EP 2003-724540		20030509
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
JP 2005534632	T	20051117	JP 2004-503003		20030509
MX 2004PA11093	A	20050214	MX 2004-PA11093		20041109
PRIORITY APPLN. INFO.:			US 2002-379517P	P	20020510
			US 2002-422272P	P	20021029
			WO 2003-US14628	W	20030509

OTHER SOURCE(S): MARPAT 139:395952
GI



I



II

AB Compds. are disclosed, which function as melanocortin receptor ligands (no data), and which have utility in the treatment of melanocortin receptor-based disorders. The compds. have structure I [q = 1 or 2; p = 1-3; W, Q, Y, Z = CH or N, provided that ≤ 2 are N, and that when 2 are N, then the N atoms are not adjacent; Ar = (un)substituted Ph or naphthyl; X = bond, O, S, N(R6a), N(R6a)C(O), N(R6a)S(O)2, N(R6a)C(O)N(R6b), C(O)O, OC(O), N(R6a)C(O)N(R6b)O, N(R6a)C(O)N(R6b)N(R6c), or N(R6a)C(O)O; R1, R2, R3a, R3b = H, (un)substituted alkyl, aryl, arylalkyl, heterocyclyl, or heterocyclylalkyl; R4a and R4b = optional ring substituents selected from OH, (un)substituted alkyl, cyano, halo, alkoxy, or alkylamino; R5 = H, (un)substituted alkyl, aryl, or heterocyclyl; R6a, R6b, R6c = H, (un)substituted alkyl; R7a, R7b = optional ring substituents selected from H and (un)substituted alkyl; provided that when p = 1 then R1, R2, R3a, and R3b cannot all be H; including stereoisomers, prodrugs, and pharmaceutically acceptable salts]. Pharmaceutical compns. containing I, as well as methods relating to their use, are also disclosed. Approx. 450 examples of compds. I and salts were prepared, as well as various intermediates. For instance, 1-Cbz-piperazine was N-arylated with 2-fluorobenzaldehyde (53%), followed by reductive amination of the aldehyde with 2-thiopheneethanamine, N-protection of the chain amino as the BOC derivative (82%, 2 steps), hydrogenolysis of CBZ (35%), peptide coupling with D-N-Fmoc-4-chlorophenylalanine using EDC, removal of Fmoc (87%, 2 steps), another peptide coupling with N-BOC-β-alanine, and removal of BOC, to give invention compound II, isolated as the trifluoroacetate salt.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:261005 CAPLUS
DOCUMENT NUMBER: 138:281147
TITLE: Methods and compounds for modulating melanocortin receptor ligand binding and activity

INVENTOR(S): Millhauser, Glenn L.; Thompson, Darren; Bolin, Kimberly; Anderson, D. Joe; McNulty, Joseph C.
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: U.S. Pat. Appl. Publ., 67 pp., Cont.-in-Part of Appl. No. PCT/US99/25201.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20030064921	A1	20030403	US 2001-851586	20010508
WO 2001030808	A1	20010503	WO 1999-US25201	19991027
W: CA, JP, US				

PRIORITY APPLN. INFO.: WO 1999-US25201 A2 19991027
US 2000-203071P P 20000509
US 2000-226047P P 20000816
OTHER SOURCE(S): MARPAT 138:281147
AB The invention relates to methods and agonist/antagonist compds. for modulating melanocortin receptor-ligand binding. Also included is a method of identifying agonists and/or antagonists that bind to a ligand binding site for a melanocortin receptor of interest. Agonists and antagonists of ligand binding to melanocortin receptors also are provided. The invention is exemplified by identification and manipulation of the C-terminus of the human agouti related protein, which binds melanocortin receptors 3 and 4, and the production of AGRP peptidomimetics that are melanocortin receptor ligands. The methods can be applied to other melanocortin receptor agonists and antagonists.

L4 ANSWER 7 OF 12 WPIDS COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-278439 [27] WPIDS
CROSS REFERENCE: 2004-624560; 2004-634430; 2004-813071; 2005-417041; 2005-434420; 2005-570485; 2007-072579; 2007-173354; 2007-173355; 2007-736582
DOC. NO. CPI: C2003-072771 [27]
DOC. NO. NON-CPI: N2003-221134 [27]
TITLE: Deriving a peptidomimetic of a metallopeptide, useful e.g. as melanocortin modulators, by designing a non-peptide cyclic molecule that mimics the template space in the peptide
DERWENT CLASS: B02; B03; S03
INVENTOR: RAJPUROHIT R; SHARMA S D; SHI Y; WU Z
PATENT ASSIGNEE: (PALA-N) PALATIN TECHNOLOGIES INC
COUNTRY COUNT: 96

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2003013571	A1	20030220	(200327)*	EN	168[0]	
EP 1425029	A1	20040609	(200438)	EN		
US 20040152134	A1	20040805	(200452)	EN		
US 20040171520	A1	20040902	(200458)	EN		
AU 2002331064	A1	20030224	(200461)	EN		
JP 2005504043	W	20050210	(200511)	JA	316	
AU 2002331064	B2	20070823	(200780)	EN		
US 7326707	B2	20080205	(200812)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003013571 A1		WO 2002-US25574	20020812
US 20040152134 A1	Provisional	US 2001-311404P	20010810
US 20040171520 A1	Provisional	US 2001-311404P	20010810
AU 2002331064 A1		AU 2002-331064	20020812
AU 2002331064 B2		AU 2002-331064	20020812
EP 1425029 A1		EP 2002-768507	20020812
EP 1425029 A1		WO 2002-US25574	20020812
US 20040152134 A1	CIP of	WO 2002-US25574	20020812
US 20040171520 A1	Cont of	WO 2002-US25574	20020812
JP 2005504043 W		WO 2002-US25574	20020812
JP 2005504043 W		JP 2003-518577	20020812
US 20040152134 A1		US 2004-761889	20040121
US 20040171520 A1		US 2004-776419	20040210
US 7326707 B2	Provisional	US 2001-311404P	20010810
US 7326707 B2	CIP of	WO 2002-US25574	20020812
US 7326707 B2	Provisional	US 2003-441139P	20030117
US 7326707 B2		US 2004-761889	20040121

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
EP 1425029	A1	Based on	WO 2003013571	A
AU 2002331064	A1	Based on	WO 2003013571	A
JP 2005504043	W	Based on	WO 2003013571	A
AU 2002331064	B2	Based on	WO 2003013571	A

PRIORITY APPLN. INFO: US 2001-311404P 20010810
WO 2002-US25574 20020812
US 2004-761889 20040121
US 2004-776419 20040210
US 2003-441139P 20030117

AN 2003-278439 [27] WPIDS

CR 2004-624560; 2004-634430; 2004-813071; 2005-417041; 2005-434420; 2005-570485; 2007-072579; 2007-173354; 2007-173355; 2007-736582

AB WO 2003013571 A1 UPAB: 20060119

NOVELTY - Deriving a peptidomimetic (I) of a metallopeptide (II) is new.

DETAILED DESCRIPTION - Deriving a peptidomimetic (I) of a metallopeptide (II) containing at least one peptide sequence (PS) complexed to a metal ion (M), where the biological activity is related to at least two elements, independently an amino acid (aa) residue or an aa side chain, or their derivatives. M is complexed to at least 3 atoms of PS, present in at least two aa, with these atoms and M forming a structural component of at least one ring which defines a template space (TS). A non-peptide ring structure (A) that is superimposable on TS is modeled and (I) is formed by adding to (A) at least 2 aa, aa side chains or derivatives such that at least 2 elements occupy a similar descriptor space as the corresponding elements in (II).

INDEPENDENT CLAIMS are also included for the following;

(1) (I) produced by the new method;

(2) melanocortin-receptor specific (I) of formula (II) or (III);

(3) peptidomimetic (Ia) comprising a TS having specified ring structures;

(4) peptidomimetic with a structure comprising a ring structure flanked by aminoacids side chains or their mimetics;

(5) peptidomimetics of formulae (a)-(d); and

(6) method for deriving peptidomimetics that bind to a selected

target.
X1 = (CH2)m or X3;
X2 = CH2, CH, NH or N;
X3 = (CH2)n, CH, NH, N, O, CO, CS, S, SO or SO2;
R5 = any group other than hydrogen;
R6 = amino acid side chain or derivative;
R7 = one or more amino acid residues or derivatives and optionally a terminal group, or is an amino acid side chain or derivative;
n = 0-3;
m = 0 or 1;
R1a = a group of formulae (i) - (iv);
R2 = 4-(amino or guanidino)butyl;
R2a = (CH2)4NH2, (CH2)3NHC(NH2)=NH, (CH2)3NHCOCH3, (CH2)3NHCOOCH3, (CH2)2NHC(NH)=NH, (CH2)2NHCONH2, (CH2)4NHCOH, (CH2)4NHCOCH3, (CH2)3NHCONHCH3, (CH2)3NHSO2NH2, (CH2)3NHSO2CH3, (CH2)3NH2, (CH2)2CONH2, (CH2)3NH(C=NH)NHMe, (CH2)3NH(C=NH)NHEt, (CH2)3NH(C=NH)NHPr, (CH2)3NH(C=NH)NHPr-i, (CH2)3NH(C=NH)NH2, (CH2)4NHCONH2, (CH2)4NH(C=NH)NH2 or a group of formulae (v) - (xiii);
R3 = R5a-R4-;
R4 = L- or D-Phe, optionally substituted by 4-(chloro, fluoro, bromo, trifluoromethyl, iodo, methyl or nitro), 2-chloro, 2,4- or 3,4-dichloro, 3,4-di(fluoro or methoxy); and
R5a = L- or D-His, Ser(benzyl), Tic (1,2,3,4-tetrahydroisoquinolime-3-carboxylic acid), heptanoyl-Ser(benzyl), Hyp(hydroxyproline)(benzyl, 2-napthyloxy, phenoxy), 4-or 5-phenyl-Pro, Tiq (1-caroxylic acid analog of Tic), Atc(2-aminotetralin-2-carboxylic acid), Igl (indanylglycine), 2-Aic (2-aminoindane-2-carboxylic acid), Idc (indoline-2-carboxylic acid), 1-Aic, NH2(CH2)6CO-, benzyl, beta-homoSer(benzyl), or Ser(2-naphthyoloxy, phenoxy, 4- or 2-chlorophenoxy).
Provided that any two adjacent CH and/or NH groups may form a double bond.
ACTIVITY - Cytostatic; Anorectic; Hypotensive; Cardiant; Dermatological; Antiseborrheic; Antiinflammatory.
Test methods are described but no results are given.
MECHANISM OF ACTION - Melanocortin agonist or antagonist (especially), angiotensin, vasopressin or oxytocin receptors. The compound 1-(His-D-Phe)-2-(3-guanidinopropyl)-5-(naphth-2-yloxy)-hexahydro-pyrrolo(1,2-a)imidazol-3-one, at 1 micro M, showed 99 %, 30 %, 69 % and 28 % inhibition at the melanocortin 1, 3, 4 and 5 receptors, respectively, in a competitive assay against alpha-MSH.
USE - The method is used to produce (I) that bind to selected targets, particularly the melanocortin (especially), angiotensin, vasopressin or oxytocin receptors, as either agonist or antagonist. (I) active at melanocortin receptors are potentially useful, in human or veterinary medicine, for diagnosis and treatment of melanoma; regulation of energy homeostasis (treatment of obesity and anorexia); treatment of sexual dysfunction; regulation of blood pressure and heart rate; as tanning agents; for regulating inflammatory processes and for treating acne.
ADVANTAGE - The method identifies receptor-specific, non-metallic scaffold molecules which may be either agonists or antagonists (contrast known methods that are generally limited to identifying antagonists).

L4 ANSWER 8 OF 12 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2003404052 EMBASE
TITLE: Clinically validated peptides as templates for de novo peptidomimetic drug design at G-protein-coupled receptors.
AUTHOR: Jones, Robert M (correspondence); Boatman, P. Douglas; Semple, Graeme; Shin, Young-Jun; Tamura, Susan Y.
CORPORATE SOURCE: Department of Medicinal Chemistry, Arena Pharmaceuticals,

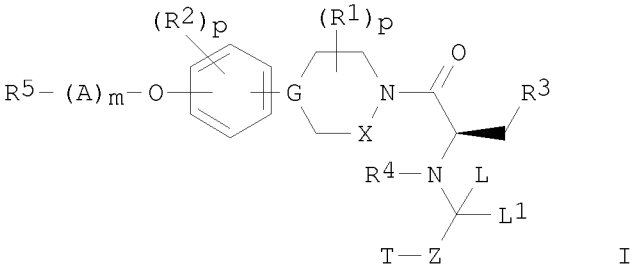
6166 Nancy Ridge Drive, San Diego, CA 92121, United States.
rjones@arenapharm.com
SOURCE: Current Opinion in Pharmacology, (Oct 2003) Vol. 3, No. 5, pp. 530-543.
Refs: 78
ISSN: 1471-4892 CODEN: COPUBK
PUBLISHER IDENT.: S 1471-4892(03)00127-9
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 029 Clinical and Experimental Biochemistry
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 23 Oct 2003
Last Updated on STN: 23 Oct 2003
AB Recent advances in the development of potent and selective peptide and non-peptide ligands for peptidergic receptors are anticipated to help further unravel the roles of class I and II G-protein-coupled receptors in the pathogenesis of human diseases and to accelerate the clinical utility of small molecule peptidomimetics. Peptidomimetic drug discovery directed towards somatostatin agonists, urotensin II antagonists, gonadotropin-releasing hormone antagonists, neurotensin and complement C5a modulators, melanocortin-4 agonists and vasopressin V(2) agonists has achieved success through integration of conformational-based drug design, site-directed mutagenesis, screening, combinatorial chemistry and classical medicinal chemistry. Acceptance that discreet ensembles of secondary structural motifs underpin the interactions of peptides with their cognate receptors has enabled the development of molecules which mimic or stabilize such pharmacophores.

L4 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:575075 CAPLUS
DOCUMENT NUMBER: 137:140779
TITLE: Preparation of piperazine- and piperidine-derivatives as melanocortin receptor agonists
INVENTOR(S): Briner, Karin; Doecke, Christopher William; Mancoso, Vincent; Martinelli, Michael John; Richardson, Timothy Ivo; Rothhaar, Roger Ryan; Shi, Qing; Xie, Chaoyu
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 272 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002059117	A1	20020801	WO 2002-US515	20020123
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2432985	A1	20020801	CA 2002-2432985	20020123

AU 2002235322	A1	20020806	AU 2002-235322		20020123
EP 1370558	A1	20031217	EP 2002-701922		20020123
EP 1370558	B1	20050824			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004523530	T	20040805	JP 2002-559419		20020123
AT 302773	T	20050915	AT 2002-701922		20020123
ES 2246390	T3	20060216	ES 2002-714719		20020123
ES 2247298	T3	20060301	ES 2002-701922		20020123
US 20040082590	A1	20040429	US 2003-466248		20030711
US 7186715	B2	20070306			
IN 2003KN00948	A	20050311	IN 2003-KN948		20030723
PRIORITY APPLN. INFO.:			US 2001-263471P	P	20010123
			WO 2001-US515	W	20020123
			WO 2002-US515	W	20020123

OTHER SOURCE(S): MARPAT 137:140779
GI



I

AB The compds. of formula I [G = CR1, or N; A = alkyl, or cycloalkyl; L and L1 = H, or (together) oxo ; T = substituted indolyl, or pyrazinyl; X = CH2, or CH2CH2; Z = (CH2)n; R1 = H, alkyl, Ph, alkylaryl, alkylcarboxamide, cycloalkyl, or oxo; R2 = H, halo, alkyl, alkylsulfonyl, cycloalkyl, alkylaryl, or haloalkyl; R3 = (un)substituted aryl, or thienyl; R4 = H, alkyl, cycloalkyl, etc.; R5 = NH2, NPh2, alkylamide, alkylsulfonylamide, NHCOH, NHCONH2, NHSO2NH2, (un)substituted heterocyclyl, etc.; n = 0-8, m = 0-1, and p = 0-4], pharmaceutically acceptable salts, or stereoisomers were prepared as melanocortin receptor agonists for treatment of obesity, diabetes and male and/or female sexual dysfunction. Thus, coupling of 2-[(2-tert-butoxycarbonyl-1,2,3,4-tetrahydroisoquinolin-3-ylmethyl)amino]-3-(4-chlorophenyl)propionate with 3-(2-piperazin-1-yltrifluoromethylphenoxy)-S-pyrrolidine-1-carboxylic acid tert-Bu ester, followed by deprotection and addition of HCl, gave 3-D-(4-chlorophenyl)-1-[4-[5-trifluoromethyl-2-S-(pyrrolidin-3-yloxy)phenyl]piperazin-1-yl]-2-D-[(1,2,3,4-tetrahydroisoquinoline-3-ylmethyl)amino]propan-1-one hydrochloride in 84% yield.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 12 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2002466438 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12224952
TITLE: A solid-phase approach to mouse melanocortin receptor agonists derived from a novel thioether cyclized peptidomimetic scaffold.
AUTHOR: Bondebjerg Jon; Xiang Zhimin; Bauzo Rayna M;

Haskell-Luevano Carrie; Meldal Morten
CORPORATE SOURCE: Contribution from the Department of Chemistry, Carlsberg Laboratory, Gamle Carlsberg Vej 10, DK-2500 Valby, Denmark.
CONTRACT NUMBER: R01-DK57080 (United States NIDDK)
SOURCE: Journal of the American Chemical Society, (2002 Sep 18) Vol. 124, No. 37, pp. 11046-55.
Journal code: 7503056. ISSN: 0002-7863.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200210
ENTRY DATE: Entered STN: 13 Sep 2002
Last Updated on STN: 26 Oct 2002
Entered Medline: 24 Oct 2002

AB The solid-phase synthesis of a novel thioether cyclized peptidomimetic scaffold, displaying functionality at the i to i + 3 positions, is reported. The thioether bridge is formed on-bead by an intramolecular reaction between a chloroacetylated reduced peptide bond and the free thiol from a cysteine. The crude products were obtained in moderate to very high purity. A series of 19 compounds were prepared and tested for agonist activity at the mouse melanocortin receptors 1, 3, 4, and 5 (mMC1-5R). From these results, several compounds were identified as having low micromolar agonist activity at the mMC1R and mMC4R. The former is involved in skin pigmentation and animal coat coloration. The latter is involved in the regulation of appetite and food intake and is currently a drug target for potential treatment of obesity. The most potent compound 1n with the pharmacophore motif "His-DPhe-Arg-Trp" was identified as having an EC(50) value of 165 nM at mMC1R, 7600 nM at mMC3R, 650 nM at mMC4R, and 335 nM at mMC5R. In addition, some of the compounds showed moderate selectivity for the mMC1R.

L4 ANSWER 11 OF 12 WPIDS COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2001-218369 [22] WPIDS
DOC. NO. CPI: C2001-065203 [22]
DOC. NO. NON-CPI: N2001-155657 [22]
TITLE: Novel construct for therapeutic use, comprising metal ion-binding domain with residues forming ligand for complexing metal ion, is conformationally constrained in structure specific for melanocortin receptors
DERWENT CLASS: B04; S03
INVENTOR: CAI H; SHARMA S D; SHI Y; YANG W; CAI H Z; SHI Y Q
PATENT ASSIGNEE: (PALA-N) PALATIN TECHNOLOGIES INC
COUNTRY COUNT: 92

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2001013112	A1	20010222	(200122)*	EN	80[11]	
AU 2000058742	A	20010313	(200134)	EN		
EP 1208377	A1	20020529	(200243)	EN		
JP 2004519410	W	20040702	(200443)	JA	150	
AU 2005201166	A1	20050505	(200540)#	EN		
US 7049398	B1	20060523	(200635)	EN		
US 20060240481	A1	20061026	(200671)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE

WO 2001013112 A1	WO 2000-US16396 20000615
US 7049398 B1 Provisional	US 1999-148994P 19990813
AU 2000058742 A	AU 2000-58742 20000615
AU 2005201166 A1 Div Ex	AU 2000-58742 20000615
EP 1208377 A1	EP 2000-944681 20000615
EP 1208377 A1	WO 2000-US16396 20000615
JP 2004519410 W	WO 2000-US16396 20000615
US 7049398 B1	WO 2000-US16396 20000615
JP 2004519410 W	JP 2001-517163 20000615
US 7049398 B1	US 2002-49718 20020213
AU 2005201166 A1	AU 2005-201166 20050317
US 20060240481 A1 Provisional	US 1999-148994P 19990812
US 20060240481 A1 Div Ex	WO 2000-US16396 20000615
US 20060240481 A1 Div Ex	US 2002-49718 20020213
US 20060240481 A1	US 2006-419557 20060522

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
AU 2000058742	A	Based on	WO 2001013112	A
EP 1208377	A1	Based on	WO 2001013112	A
JP 2004519410	W	Based on	WO 2001013112	A
US 7049398	B1	Based on	WO 2001013112	A
US 20060240481	A1	Div ex	US 7049398	B

PRIORITY APPLN. INFO: US 1999-148994P 19990812
US 1999-148994P 19990813
US 2002-49718 20020213
AU 2005-201166 20050317
WO 2000-US16396 20000615
US 2006-419557 20060522

AN 2001-218369 [22] WPIDS

AB WO 2001013112 A1 UPAB: 20060116

NOVELTY - A construct (I) comprising a metal ion-binding domain comprising two or more linked residues forming an N3S1 ligand available for complexing with a metal ion, where (I) is conformationally constrained in a structure specific for one or more melanocortin receptors (MC) upon complexing the metal ion-binding domain with a metal ion, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a manufactured peptide (II) and its salt comprising a metal ion-binding domain comprising two or more contiguous amino acids and a determined biological function domain specific for one or more MCs, where at least a portion of the biological-function domain is co-extensive with at least a portion of the metal ion-binding domain, and where the biological-function domain is conformationally constrained upon complexing the metal ion-binding domain with a metal ion; and

(2) a combinatorial library (III) targeted to MC of different sequence peptide or peptidomimetic members synthesized on solid phase or in solution, where each constituent library member comprises: (a) a peptide or a peptidomimetic sequence of three or more amino acid residues and mimics of amino acid residues bound to solid phase characterized by, (i) a sequence of two or more amino acid residues, or their mimics or combinations forming a metal ion-binding domain and including at least one amino acid residue or its mimic containing at least one S, where the S is protected by an orthogonal S-protecting group, (ii) a sequence of one or more amino acid residues, or their mimics or combinations at the N- or C- terminus of the metal ion-binding domain, or at both the N- and C-terminus of the metal ion-binding domain, and optionally, (iii) a cleavable bond attaching the peptide or peptidomimetic sequence to solid phase; and (b) a unique selection

or sequence of amino acid residues, or their mimics or combinations, in the peptide or peptidomimetic sequence of at least one of the constituent members of the library, where the orthogonal S-protecting group may be removed without cleaving the peptide or peptidomimetic sequence from the solid phase.

ACTIVITY - Antiinflammatory; Cytostatic; Anorectic; Vasotropic; Dermatological.

MECHANISM OF ACTION - None given.

USE - (I), (II) or (III) are useful for treating obesity and related pathologic conditions, melanoma, eating disorders such as anorexia, inflammation and sexual dysfunction, including treatment of both male erectile dysfunction and female sexual dysfunction. (I), (II) or (III) are useful for diagnosing, including imaging and staging melanoma tumors and metastases, as chemoprevention agent for combating harmful sun or UV exposure that induces neoplastic activity in skin melanocytes, including sun light-induced DNA damage in the skin, and as a tanning agent.

L4 ANSWER 12 OF 12 WPIDS COPYRIGHT 2008 THE THOMSON CORP on STN

ACCESSION NUMBER: 2000-442392 [38] WPIDS

CROSS REFERENCE: 1997-077237; 2003-046721; 2003-596563; 2004-119115; 2005-596282

DOC. NO. CPI: C2000-134554 [38]

TITLE: New metallopeptide or metallopeptidomimetic combinatorial libraries, useful for identifying agents which bind a target molecule or mediate a biological activity

DERWENT CLASS: B04; D16

INVENTOR: SHARMA S D; SHI Y

PATENT ASSIGNEE: (PALA-N) PALATIN TECHNOLOGIES INC; (SHAR-I) SHARMA S D; (SHIY-I) SHI Y

COUNTRY COUNT: 88

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2000036136	A1	20000622	(200038)*	EN	54[5]	
AU 2000020541	A	20000703	(200046)	EN		
EP 1141375	A1	20011010	(200167)	EN		
US 20020012948	A1	20020131	(200210)	EN		
JP 2002536295	W	20021029	(200274)	JA	76	
AU 760257	B	20030508	(200337)	EN		
US 20060003386	A1	20060105	(200603)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000036136	A1	WO 1999-US29743	19991214
US 20020012948	A1 Provisional	US 1998-112235P	19981214
EP 1141375	A1	EP 1999-964263	19991214
EP 1141375	A1	WO 1999-US29743	19991214
JP 2002536295	W	WO 1999-US29743	19991214
AU 2000020541	A	AU 2000-20541	19991214
AU 760257	B	AU 2000-20541	19991214
JP 2002536295	W	JP 2000-588384	19991214
US 20020012948	A1	US 2001-883069	20010614
US 20060003386	A1 Provisional	US 1998-112235P	19981214
US 20060003386	A1 Div Ex	US 2001-883069	20010614
US 20060003386	A1	US 2005-221210	20050907

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 760257 B	Previous Publ	AU 2000020541 A
AU 2000020541 A	Based on	WO 2000036136 A
EP 1141375 A1	Based on	WO 2000036136 A
JP 2002536295 W	Based on	WO 2000036136 A
AU 760257 B	Based on	WO 2000036136 A

PRIORITY APPLN. INFO: US 1998-112235P 19981214
WO 1999-US29743 19991214

AN 2000-442392 [38] WPIDS

CR 1997-077237; 2003-046721; 2003-596563; 2004-119115; 2005-596282

AB WO 2000036136 A1 UPAB: 20060206

NOVELTY - New metallopeptide combinatorial libraries are synthesized using a sequence of 2 or more amino acids containing at least one S to form a metal ion-binding domain.

DETAILED DESCRIPTION - A novel combinatorial library of different sequence peptide members synthesized on a solid phase comprises:

(a) a peptide sequence of 3 or more amino acid residues bound to solid phase characterized by:

(i) a sequence of 2 or more amino acid residues forming a metal ion-binding domain and including at least one amino acid residue containing at least one S where the S is protected by an orthogonal S-protecting group;

(ii) a sequence of one or more amino acid residues at the N- or C-terminus of the metal ion-binding domain, or at both the N- and C-terminus of the metal ion-binding domain; and

(iii) a cleavable bond attaching the peptide sequence to solid phase; and

(b) a unique selection or sequence of amino acid residues in the peptide sequence of at least one of the constituent members of the library.

The orthogonal S-protecting group may be removed without cleaving the peptide sequence from the solid phase.

INDEPENDENT CLAIMS are also included for the following:

(1) a combinatorial library of different sequence peptidomimetic members synthesized on a solid phase, where each constituent library member comprises:

(a) a peptidomimetic sequence of a combination of 3 or more amino acid residues and mimics of amino acid residues bound to solid phase characterized by:

(i) a sequence of 2 or more amino acid residues, mimics of amino acid residues or combinations forming a metal ion-binding domain and including at least one amino acid residue or mimic of an amino acid residue containing at least one S where the S is protected by an orthogonal S-protecting group; and

(ii) a sequence of 1 or more amino acid residues, mimics of amino acid residues or combinations at the N- or C- terminus of the metal ion-binding domain, or at both the N- and C-terminus of the metal ion-binding domain; and

(iii) a cleavable bond attaching the peptidomimetic sequence to solid phase; and

(b) a unique selection or sequence of amino acid residues, mimics of amino acid residues or combinations in the peptidomimetic sequence of at least one of the constituent members of the library (where the orthogonal S-protecting group may be removed without cleaving the peptidomimetic sequence from the solid phase);

(2) a combinatorial library of different sequence peptide or peptidomimetic members synthesized in solution, where each constituent library member comprises:

(a) a peptidomimetic sequence of a combination of 3 or

more amino acid residues and mimics of amino acid residues bound to solid phase characterized by:

(i) a sequence of 2 or more amino acid residues, mimics of amino acid residues or combinations forming a metal ion-binding domain and including at least one amino acid residue or mimic of an amino acid residue containing at least one S where the S is protected by an orthogonal S-protecting group; and

(ii) a sequence of one or more amino acid residues, mimics of amino acid residues or combinations at the N- or C-terminus of the metal ion-binding domain, or at both the N- and C-terminus of the metal ion-binding domain; and

(b) a unique selection or sequence of amino acid residues, mimics of amino acid residues or combinations in the peptidomimetic sequence of at least one of the constituent members of the library;

(3) a method for generating a metallopeptide or metallopeptidomimetic combinatorial library comprising:

(a) constructing a library containing sequences of the formula Aaa-MBD-Baa cleavably bound to a solid phase, where:

(i) MBD comprises at least 2 amino acid residues, mimics of amino acid residues or combinations, with at least one of the residues comprising at least one nitrogen atom available to complex with the coordination sphere of a metal ion, the metal ion to be provided, and with at least one of the residues comprising at least one sulfur atom protected by an orthogonal S-protecting group; and

(ii) Aaa and Baa each comprise 0-20 amino acid residues, mimics of amino acid residues or combinations, provided that Aaa and Baa comprise at least 1 amino acid residue or mimic of an amino acid residue, and provided that between at least 2 of the sequences of the formula Aaa-MBD-Baa at least either Aaa or Baa differ in at least either the sequence of residues or the selection of residues;

(b) deprotecting the sulfur atom protected by an orthogeonal S-protecting group by cleaving the orthogonal S-protecting group without cleaving the sequence from the solid phase; and

(c) complexing a metal ion to the MBD (where the resulting metal ion-complexed sequences form a metallopeptide or metallopeptidomimetic combinatorial library); and

(4) a method for producing pure metallopeptides or metallopeptidomimetics without a solution purification step comprising:

(a) synthesizing a sequence of formula Aaa-MBD-Baa cleavably bound to solid phase, where:

(i) MBD comprises at least 2 amino acid residues, mimics of amino acid residues or combinations, with at least one of the residues comprising at least one nitrogen atom available to complex with the coordination sphere of a metal ion, the metal ion to be provided, and with at least one of the residues comprising at least one sulfur atom protected by an orthogonal S-protecting group; and

(ii) Aaa and Baa each comprise 0-20 amino acid residues, mimics of amino acid residues or combinations;

(b) deprotecting the sulfur atom protected by an orthogonal S-protecting group by cleaving the orthogonal S-protecting group without cleaving the sequence from the solid phase;

(c) complexing a metal ion to the MBD;

(d) cleaving the metal ion-complexed sequence from the solid phase; and

(e) recovering the resulting pure metal ion-complexed sequence.

USE - The methods can be used for providing metallopeptide or metallopeptidomimetic combinatorial libraries. In each of the methods and libraries provided, a specific conformational restriction is obtained upon complexing the peptides or amino acid sequences with a metal ion, such that the conformationally constrained peptide-metal ion complexes can serve as surrogates for reverse turn structures, such as beta turns and gamma turns commonly found in naturally occurring peptides and proteins.

The turns formed as a consequence of metal ion complexation are more stable than the naturally occurring turn structures, which are stabilized only by weaker interactions such as Van der Walls' interactions and hydrogen bonds. The libraries can be used for the identification and characterization of library constituents which are capable of binding a target molecule of interest, or mediating a biological activity of interest.

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=> FIL STNGUIDE
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                      72.83      73.04

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                      -4.00      -4.00

FILE 'STNGUIDE' ENTERED AT 11:12:10 ON 09 APR 2008
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Apr  4, 2008 (20080404/UP).

=>
=> d his

     (FILE 'HOME' ENTERED AT 11:07:10 ON 09 APR 2008)

     FILE 'MEDLINE, BIOSIS, CAPLUS, SCISEARCH, EMBASE, WPIDS' ENTERED AT
     11:07:34 ON 09 APR 2008
L1          3147 MELANOCORTIN (S) RECEPTOR AND (TREAT OR TREAT? OR THERAP?)
L2             0 PETIDOMIMETIC AND L1
L3            19 PEPTIDOMIMETIC AND L1
L4            12 DUP REM L3 (7 DUPLICATES REMOVED)

     FILE 'STNGUIDE' ENTERED AT 11:12:10 ON 09 APR 2008

=> logoff y
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       3.18      76.22

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                       0.00      -4.00

STN INTERNATIONAL LOGOFF AT 11:43:48 ON 09 APR 2008
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